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The Bulletin *of the*
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May, 1922

DIABETES INSIPIDUS, ITS PATHOGENESIS AND THERAPEUTICS

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From the Medical Clinic, Lund, Sweden.—Professor Karl Petrén

As early as 1916 (1) I had an opportunity of demonstrating a case of diabetes insipidus before the Medical Society of Lund. Careful study of the case led to the conclusion that current views of the disease need revision. Diabetes insipidus is rare in this part of the country, and since the occasion mentioned only two cases have been admitted to the Clinic. The opportunity to study these cases was limited.

Diabetes insipidus, here defined by its most prominent symptom, a polyuria with no other noticeable changes in the urine, is a phenomenon of human pathology that has been recognized for a long time. However, until the researches of Tallqvist (2) and Meyer (3), 15-20 years ago, diabetes insipidus was but a common name for a group of diseases of the most varied etiology, in which the predominant symptom was merely an increased excretion of urine.

Tallqvist ascribed the polyuria of diabetes insipidus not to increased activity of the kidneys, but to lack of power on the part of the kidneys to secrete urine with normal NaCl and N percentage. Meyer also considers that in diabetes insipidus verus, as distinguished from the polyuria arising after a primary poly-

dipsia, there is present a loss of concentrating power for all the "harnfähigen Stoffen" collectively.

Veil (4) has, however, lately denied the value of the tests which have hitherto been considered convincing for establishing the presence of a primary polyuria, viz., the obvious diminution in the quantity, but maintained concentration, of the urine when the saline and protein ingredients in the food are reduced, and, on the other hand, an increased diuresis—in this case also without any remarkably noteworthy increase in the concentration—after the introduction on a single occasion of a larger quantity of sodium chloride. According to his view, which is founded upon extremely interesting researches into which lack of space unfortunately forbids me to enter, it is only by a strict limitation of the supply of fluid, a thirst-experiment in other words, that it is possible to form an idea as to whether in a given case of "diabetes insipidus" there is any restriction in the concentrating power of the kidneys. The patient whom I had under observation has satisfied the requirements which Meyer and Veil formulated as decisive for the diagnosis of a true diabetes insipidus. The history of his disease offers nothing remarkable and can be told in a few words.

A man—Journ. No. 108, 1916—twenty years of age, with a clean health record and presenting no hereditary features of interest, experienced during the early days of October, 1915, a gradually increasing feeling of thirst. At the same time polyuria, but with no special urinary inconvenience noted. A careful and comprehensive objective examination revealed nothing of interest, excepting some ulcerations with abrupt margin in the gluteal region, on the thighs, and the shin of the right leg. The Wassermann reaction was positive in the blood serum. The cerebro-spinal fluid was not pathologically changed, and on the cranial skiagram nothing abnormal could with certainty be detected. The urine, which contained no abnormal constituents, was light in color and had a specific gravity of 1,002.

Before admission into the hospital the patient had lived on ordinary food. A reduction of albumen and salt in the diet brought about a considerable diminution in the secretion of urine (Table I). On a diet of unsalted butter, bread, gruel, pork (rib portion), vegetables, potatoes, apples, and 1 gm. of salt, the quantity of urine decreased from 11 or 12 to 8 or 9 litres, and further to 7 litres, when a few days later the gram of salt was omitted.

During the whole time the total concentration of the urine remained almost on the same level, the specific gravity being about 0:001 and the freezing-point depression showing values varying between 0.12 and 0.08. In a normal individual under a similar experiment the quantity of urine—independently of the reduction of albuminous and saline foodstuffs—would have remained on the whole at about the same level as before, while the concentration would have diminished. This difference already makes it plausible that an impaired power of concentration in the kidneys is present, a probability which experimental

evidence shows to be a demonstrable fact, as will appear from the following.

On March 7 the patient was given in the course of the day 20 gm. of sodium chloride, administered to him partly in his food, partly in teaspoonfuls dissolved in water, with the result that the quantity of urine increased from 6,300 c.c. during the preceding 24 hours to 8,110 c.c., or nearly 2 litres (Table II). On the following days also the urine maintained a fairly high level—the day after, 7,500, and afterwards, 7,000 c.c. The concentration of the urine, on the other hand, was unchanged. A distinct retention of the salt took place, and not until nearly a week after its introduction, when the 24-hour quantities had reached the same level as before the beginning of the experiment, could it be considered to be completely eliminated. The accelerated diuresis during the period of March 8-12 also must in all probability be ascribed to the protracted excretion of the salt. As soon as the organism had recovered its equilibrium in regard to sodium chloride, the urine decreased to the same quantity as before the introduction of the salt. An interesting observation is that the percentage of the sodium chloride rises during the first few days after its introduction, which, therefore, shows that the kidneys do not, as a rule, use their utmost capacity of concentration, but are able under certain conditions to present a greater. The study of the various portions of urine during periods of 24 hours leads to the same view. It appears, namely, that the morning urine presents a higher degree of concentration than the urine passed later in the day.

On one occasion (9/1, 1916) the patient was rigorously restricted with regard to supply of liquid (1,500 c.c.). The low specific gravity (1.002) found in the urine during this day argues to some extent for the presence of a genuine diabetes insipidus. On this day, as well as the following, when the patient by no slight exertion of will-power succeeded in limiting his intake of fluids, the specific gravity did not reach higher values than during the time when he took fluids *ad libitum*. Even supposing that in the hourly testing of the urine during the "day of thirst" an increased concentration might have been found in some single portion, there can under no circumstances be any question of a considerable increase, inasmuch as in that case there would have appeared in some degree a rise in the specific gravity for the total 24 hours.

On a later occasion—17/2, 1917—when the patient came back to the hospital to undergo treatment for syphilis, a regular thirst-experiment was undertaken. With the usual diet he then passed a good 4 litres of urine with specific gravity 1.005. On 21/2, 1917, the patient from the time of awaking to 7 p.m. received only 500 c.c. of fluid. The previous night he had received about 12 c.c. Further attempts to restrict the amount of fluid were frustrated by the patient's refusal to submit to the treatment. The night urine amounted to 800 c.c.; in the daytime he passed 1,350 c.c. The specific gravity of the morning urine was 1.0085 and rose during the day to 1.0145 at most. The maximum concentration of NaCl and N amounted to 0.61 and 1.32 per cent respectively. Of special interest is it to note that the specific gravity does not increase in uniform progression, but shows after 1 p.m. a distinct tendency to fall, and this in spite of the fact that the patient after 4 p.m., by which time the quantity of liquid allowed had been consumed, was given nothing more to drink until 7 p.m. A particularly noteworthy fact is that the diminishing specific gravity is caused by a gradual reduction of the sodium chloride concentration. Thus an impaired power of concentration is manifested also by this experiment.

Considering myself, therefore, fully justified in pronouncing the present case to be one of genuine diabetes insipidus—even in accordance with the demands made by Veil—I now revert to the discussion of the pathogenesis of this disease. The view maintained by Meyer that the essence of the disease is to be sought

TABLE I.

Day	Diet	Urine						Blood	
				NaCl		N			
		Quant. per 24 Hours C.C.	Freezing Point °C.	0/00	Total Quant. Gm.	0/00	Total Quant. Gm.	NaCl %	Sugar %
1916									
22/1	Bread, butter, milk, cream, 100 gm. meat	11,400	−0.12	1.00	11.4	0.98	11.2	0.50	0.101
23/1		12,200	−0.12	1.82	9.8	1.26	15.1	0.51	0.112
24/1		12,000	−0.12	0.70	8.4	1.12	13.2	0.50	0.112
25/1	Unsalted butter, bread, gruel, pork (rib port.), greens, potatoes, apples, salt 1 gm.	11,200	−0.11	0.96	10.8	1.26	14.1	0.50	0.100
26/1		11,500	−0.11	0.90	10.4	0.98	11.5	0.49	0.100
27/1		9,500	−0.10	0.94	8.9	1.25	11.9	0.49	0.097
28/1		10,400	−0.12	0.70	7.3	0.70	7.3	0.50	0.089
29/1		9,800	−0.10	0.62	6.3	0.63	6.2	0.50	0.095
30/1		8,700	−0.09	1.17	10.2	0.70	6.1	0.48	0.122
31/1		9,200	−0.09	0.58	5.4	1.40	12.9	0.48	0.128
1/2	Salt exc.	8,000	−0.09	0.47	3.7	0.70	5.6	0.47	0.109
2/2		7,500	−0.08	0.53	3.9	0.85	6.4	0.49	0.101
3/2		7,300	−0.08	0.58	4.3	0.85	6.2	0.49	0.107
4/2		7,300	−0.08	0.47	3.4	0.64	4.7	0.49	0.101
5/2		7,000	−0.08	0.47	3.3	1.68	11.0	0.49	0.095
6/2		7,200	−0.09	0.58	4.2	0.83	6.0	0.47	0.111

in a diminished "Gesamtleistung der Niere" proves on further investigation to be untenable. The nearest support for this view was in particular the observation that with an increased supply of albuminous food-stuffs the kidneys also reacted with an aug-

mented diuresis, but with no increase in concentration. Therefore, since the kidneys, according to this test, besides being insufficient for salt, were also inadequate for nitrogen—which, together with salt, mainly causes molecular concentration of the urine—

TABLE II.

Day 1916	Urine						Blood		
	Quant. per 24 Hours C.C.	Freezing Point, °C.	NaCl		N		NaCl %	Sugar %	Remarks
			0/00	Total Quant. Gm.	0/00	Total Quant. Gm.			
3/3	6,550	−0.11	0.64	4.2	0.84	5.5	0.48	0.112	
4/3	6,900	−0.12	0.61	4.2	0.84	5.8	0.49	0.101	
5/3	6,700	−0.11	0.89	6.0	0.99	6.6	0.49	0.100	
6/3	6,300	−0.11	0.83	5.3	0.99	6.2	0.50	0.121	
7/3	8,100	−0.12	0.82	6.6	0.70	5.7	0.49	0.113	Sodium chloride 20 gm.
8/3	7,500	−0.13	1.40	10.5	0.71	5.3	0.49	0.109	
9/3	7,000	−0.12	1.16	8.1	0.56	3.9	0.50	0.101	
10/3	7,000	−0.13	1.05	7.4	0.70	4.9	0.49	0.103	
11/3	7,000	−0.12	1.05	7.4	1.12	7.8	0.50	0.113	
12/3	7,000	−0.14	1.17	8.2	1.12	7.8	0.49	0.105	
13/3	5,075	−0.13	0.99	6.0	0.98	5.0	0.50	0.117	
14/3	6,000	−0.13	0.76	4.6	1.13	6.1	0.50	0.109	

TABLE III. 21/2, 1917. THIRST EXPERIMENT.

	Quantity of Urine C.C.	Sp. G.	N %	NaCl %
7– 8 a.m.	150	1.0085	0.29	0.41
8–10 "	350	1.0105	0.66	0.54
10–11 "	145	1.011	0.94	0.61
11– 1 p.m.	145	1.0145	1.26	0.61
1– 3 "	240	1.014	1.32	0.50
3– 5 "	175	1.013	0.99	0.41
5– 7 "	145	1.013	1.26	0.37
7– 8 p.m.	165	1.009	0.42	0.26

the conclusion was very natural. Experiments with the use of phosphoric acid on the other hand produced greatly diverging results.

Do the experiments made by the earlier authors really prove that the kidneys in an individual with diabetes insipidus are incapable of eliminating N in a concentrated form, or is some other line of explanation possible? In order to obtain an answer to this question I have submitted the recorded experimental results to a searching scrutiny, and the verdict of this criticism is that there is no doubt that a greater supply of protein has, to a considerable degree, increased the diuresis without appreciably affecting the concentration. Hence this points to the acceptance of Tallqvist's and Meyer's opinion—but only upon a superficial

TABLE IV. TALLQVIST.

Date	Body Weight (Kg.)	Total Amount of N	Quantities Eliminated						
			Urine					Faeces	Total N
			Quantity C.C.	Sp. G.	Freezing Point, °C.	NaCl		N	
						0/00	Gm.	Gm.	
Jan.									
22	66.8	22.58	3,720	1.004	-0.30	0.52	1.92	0.73	10.77
23		22.58	4,900	1.005	-0.35	0.58	2.94	0.73	13.47
24		22.58	6,050	1.005	-0.31	0.58	3.51	0.73	15.85
25		22.58	6,420	1.005	-0.32	0.59	3.11	0.73	21.27
26		22.58	7,700	1.005	-0.32	0.61	4.70	0.73	19.21
27		22.13	6,425	1.004	-0.32	0.58	3.63	0.73	21.93
28		22.13	7,850	1.004	-0.29	0.58	4.55	0.73	24.28
29		22.13	8,500	1.004	-0.29	0.60	5.10	0.73	21.98
30		22.13	7,300	1.005	-0.36	0.60	4.38	0.73	22.63
31	65.2	22.13	6,700	1.005	-0.36	0.59	3.95	0.73	21.50

view. The study of the published series of experiments in which estimations have been made both of the nitrogen and of the sodium chloride eliminated—I have been able to find no more than three—has shown that in every case *the increased supply of protein has brought about an accelerated elimination of sodium chloride*. I pass on immediately to a detailed examination of the particular researches.

Tallqvist was the first to test the capacity of the organism for eliminating nitrogen. The patient with whom he worked had for some time been placed on a certain standard diet, and was all at once given a considerable quantity of protein (22.58 gm.

N), which was continued. It was then found that in proportion as the organism adjusted itself to N the quantity of urine gradually increased from 3,720 c.c. during the first day of experiment to 8,500 c.c. At the same time the specific gravity remained unchanged at 1.004-1.005. The molecular concentration varied from -0.29° to -0.36°. I quote in Tallqvist's own words the conclusions at which he arrived from these researches: "Die Menge des Harns nimmt also zu, je nach dem der demselben mit der Nahrung zugeführte, Stickstoff immer nach und nach vollständig darin enthalten ist, und das ganze liefert einen treffenden Beweis für die grosse Rolle, welche die Menge der zur Ausscheidung bestimmten N-haltigen Produkte für die Harnabspaltung spielt."

Regarding the elimination of sodium chloride it is conspicuous that the percentage is maintained unchanged, or, if anything, there appears a slight increase. The total excretion of salt, therefore, increases considerably at the same time. I shall return to this observation.

Meyer has also adopted for his researches into diabetes insipidus a method similar to Tallqvist's. After the patient had been put on a strict diet for some time, he received an addition of 150 gm. of meat per 24 hours, which was continued for a week. On the day on which the alteration was effected, the quantity of urine increased from about 7½ litres to 10,400 c.c., and during the rest of the experimental period it amounted to 8.3-10.4 litres daily. The specific gravity presented but unimportant changes between 1.002-1.004; the freezing-point depression went down somewhat from -0.15° - -0.17° before the commencement of the experiment to -0.20° - -0.22°. Once it presented a value as low as -0.26°. On account of this reaction of the kidneys to the supply of protein, Meyer likewise concluded that these organs in a certain measure were powerless to eliminate a more concentrated nitrogenous urine.

The total elimination of sodium chloride, however, presented considerably heightened values in this case also, and that this is not an accident becomes evident from a further experiment with similar arrangements, in which as large quantities as 14 to 15 gm. NaCl were eliminated, as against values of 7-4 gm. before the addition of meat.

Finally, a Swedish author, Kahlmeter (5), has made an experiment of the same kind with a somewhat different mode of procedure in a case of diabetes insipidus. In the morning 10 gm. of urea were administered to his patient, who had already been stabilized some days previously with regard to nitrogenous constituents. As the table indicates, no increase in the specific gravity of the urine appears in this case either, while the quantity of urine, on the other hand, has increased perceptibly. The total quantity of NaCl eliminated appreciably exceeds the quantity eliminated during the 24 hours before and after the experi-

TABLE V. E. MEYER (Case I, Table II).

	Date	Urine C.C.	Sp. G.	Freezing Point, °C.	NaCl		N
					%	Gm.	Gm.
Limited diet	6/ 7X	7,600	1.003	–0.17	0.086	6.52	6.01
	7/ 8	7,600	1.002	–0.15	0.056	4.26	7.34
	8/ 9	7,450	1.003	–0.17	0.043	3.20	7.50
+ 150 gm. meat	9/10	10,400	1.002	–0.17	0.078	8.11	11.17
	10/11	10,400	1.004	–0.20	0.099	10.29	14.63
	11/12	10,180	1.004	–0.20	—	—	14.90
	12/13	9,270	1.002	–0.21	0.097	9.07	13.38
	13/14	8,800	1.002	–0.22	—	—	13.98
	14/15	8,300	1.003	–0.26	0.065	5.40	14.69
	15/16	10,000	1.002	–0.20	0.073	7.25	15.42
Limited diet	5/ 6XI	9,300	1.002	–0.17	0.100	9.30	8.07
	6/ 7	10,460	1.002	–0.15	0.070	7.32	8.05
	7/ 8	8,640	1.001	–0.15	0.084	7.26	6.70
	8/ 9	6,380	1.002	–0.16	0.060	4.03	6.07
+ 150 gm. meat	9/10	11,400	1.002	–0.19	0.150	11.97	14.41
	10/11	11,040	1.002	–0.19	0.139	15.35	10.66
	11/12	10,480	1.002	–0.20	0.134	14.04	9.61

ment. The percentage of sodium chloride in the urine remained constantly at about the same level.

The observation that in all these three cases the percentage of the sodium chloride in the urine after the introduction of protein remains unchanged, while the total quantity of sodium chloride eliminated considerably increases, is worthy of close attention.

Is it not natural to conclude that it is the increased NaCl-elimination that causes the accelerated diuresis? Sodium chloride, as is well known, cannot in these cases be eliminated

from the kidneys in a concentrated form, and since the increased supply of protein involves an accelerated elimination of salt, the natural consequence is that the urine increases in quantity in proportion to the increased elimination of sodium chloride, so that the organism may be able to excrete the mobilized quantity of salt. The consequence of this is, of course, that all other constituents of the urine will be found in a more diluted form than before.

In order to obtain a conclusive reply to this question, I have for a long period placed my patient on a diet strictly reduced as to salt and later also as to protein food, whereupon as small

TABLE VI. KAHLMETER.

Day	Nutriment					Waste Products					
	Protein	N	Water	Quantity of Urine, C.C	Sp. G.	NaCl		Urea		N	
						Gm.	%	Gm.	%	Gm.	%
23/5	56	9.8	2,700	2,500	1.004	3.45	0.15	8.75	0.35	7.5	0.30
24/5	9 a.m. 10 gm. urea per os.										
Time											
9–12 noon	—	—	—	400	1.005	0.60	0.15	1.2	0.30	1.7	0.42
12– 3 p.m.	—	—	—	750	1.003	1.12	0.15	—	—	—	—
3– 6 "	—	—	—	750	1.002	1.12	0.15	2.7	0.36	—	—
6– 9 "	—	—	—	700	1.003	1.05	0.15	—	—	—	—
9–12 midnight	—	—	—	825	1.002	1.22	0.15	2.9	0.35	2.7	0.34
12– 3 a.m.	—	—	—	550	1.003	0.55	0.10	—	—	—	—
3– 6 "	—	—	—	600	1.004	0.90	0.15	—	—	—	—
6– 9 "	—	—	—	400	1.004	0.40	0.10	1.6	0.4	—	—
Total 24 hours	58	9.3	3,500	4,975	1.003	6.96	0.13	17.9	0.36	18.8	0.38
25/5	53	8.5	2,800	3,100	1.004	4.6	0.15	12.4	0.4	11.2	0.36

quantities as 1.5 to 3 gm. sodium chloride were eliminated, after which I gave him an appreciable addition of protein food (300 gm. meat, 3 eggs, and 100 gm. cheese).

During this test the daily secretion of N rose to nearly 12 gm., as against about 4 gm. during the preceding period. Nevertheless, the quantity of urine remained invariably at the same level, while the freezing-point depression, on the other hand, presented a decided fall from -0.14° - -0.17° before the commencement of the experiment down to -0.36° during its course.

Thus my researches have led to a result which diverges absolutely from the results of previous investigators and this divergence is in all probability due to the fact that the patient—

on account of the protracted reduction of salt before the experiment—had no reserves of sodium chloride. No mobilization of sodium chloride such as might affect the diuresis has appeared as a result of the increased supply of protein, as we have seen was the case in the experiments of the authors quoted. The moderate increase of the entire quantity of sodium chloride excreted is in my case not larger than is to be explained by the addition of salt which the patient received as the result of the change in diet.

TABLE VII. AUTHOR'S EXPERIMENT.

Day	Diet	Quantity of Urine per 24 Hours C.C.	Freezing Point, °C.	N		NaCl	
				0/00	Gm.	0/00	Gm.
July 25	Fat, greens, potatoes, 150 gm. bread	3,600	–0.17	1.40	5.04	0.59	2.12
26		4,000	–0.16	0.98	3.92	0.64	2.56
27		3,200	–0.15	0.98	3.14	0.64	2.05
28		3,400	–0.14	0.98	3.33	0.64	2.18
29		4,000	–0.15	1.12	4.48	0.88	3.52
30	300 gm. meat, 3 eggs, 100 gm. cheese	4,000	–0.21	1.40	5.60	0.88	3.52
31		4,000	–0.28	1.40	5.60	1.05	4.20
Aug. 1		3,600	–0.30	2.24	8.06	0.82	2.95
2		3,400	–0.34	1.90	6.46	0.88	2.99
3		4,000	–0.32	2.80	11.20	0.82	3.28
4		4,000	–0.32	2.52	10.08	0.94	3.76
5		4,000	–0.34	2.94	11.76	0.99	3.96
6		4,000	–0.36	3.08	12.32	1.05	4.20
7		4,000	–0.36	2.66	10.64	0.99	3.96
8		4,000	–0.32	1.26	5.04	0.99	3.96
9		4,000	–0.28	2.24	8.96	0.94	3.76
10		4,000	–0.29	2.52	10.08	0.88	3.52
11		4,000	–0.30	2.52	10.08	1.05	4.20

Norgaard (6) describes a case of diabetes insipidus in which the daily quantity of urine was not "appreciably" increased after the introduction of 20 gm. of urea. This state of affairs is not improbably to be ascribed to the "saltless" diet on which the patient had for some time been living and in consequence of which the organism had been freed from the greater part of its reserves of sodium chloride. The result was that this case dif-

fered from Kahlmeter's in that the excretion of sodium chloride, too, was not "appreciably" increased.

My conclusion is that the conflicting results to which my researches and those of previous investigators have led are due to differences in the mode of conducting the experiments. If a patient with a genuine diabetes insipidus has at his disposal considerable reserves of sodium chloride in the organism, an increased supply of protein causes an accelerated elimination of salt. But if he has previously been deprived of these reserves, as a result of a sufficient reduction of sodium chloride in the food, no increased quantity of NaCl will be excreted. The manner in which the kidneys react to the increase of protein varies according to the different conditions of experiment. In the first instance he responds with a markedly increased diuresis, but with maintained concentration of urine; in the second case he reacts in the same way as a normal individual, with maintained or but slightly increased quantity of urine and rising concentration.

The close analysis of previous experiments and of the results of my own researches seems to justify my question as to whether, on the whole, there is in genuine diabetes insipidus any impaired power of concentrating N or any reduced "Gesamtleistung der Niere." At all events, no tenable proof for this is yet forthcoming, although, of course, I do not propose to deny that such cases may occur. Veil, to judge by a short review of a paper read by him before the 32nd German Congress for Internal Medicine, 1920, seems now to divide cases of diabetes insipidus into two classes—those with increased, and those with diminished NaCl-percentage in the blood, hyper- and hypo-chloraemic forms respectively.

My view that only an impaired power of concentrating NaCl occurs is to some extent borne out, in the case examined by me, by the thirst-experiment. On the day when this was carried out my patient excreted N in a concentration up to 1.32 per cent, whereas the NaCl excretion, on the contrary, did not go higher than 0.61 per cent, with a further drop to 0.37 per cent in spite of a continued reduction of liquid by regular stages. Again, the N percentage remained at the same level (See Table III).

Two more cases of diabetes insipidus which I have examined in the Clinic point in the same direction, although—as I have

already hinted—the patients' short stay in the hospital and their unwillingness to lend themselves to the experiment frustrated investigations of a more lengthy and detailed character. In the first case, No. 151/1917, when the concentration test was taken, the N-concentration reached—at a specific gravity of 1.017—a height of 1.11 per cent, while NaCl was not excreted in a higher concentration than 0.39 per cent; in the second case, No. 534/1917, the NaCl percentage kept at about the level (0.35-0.40 per cent) which it had reached during the preceding night's reduction of fluid, while the N-concentration rose in slow but steady progression from 0.43 to 0.78 per cent. The patient's positive refusal to undergo further reduction of liquid terminated the examinations, from which still more obvious proof might otherwise have been forthcoming.

Concerning the etiology of the disease, a hypothesis—based on experiments with animals and on the results of certain clinical experiences—has been adopted, namely, that diabetes insipidus originates in a hypofunction of the posterior (intermediary) pituitary lobe. That this question, however, is by no means definitely settled becomes evident from the criticism to which the Swedish author, af Klercker (7), and others have subjected the collective demonstrations of this hypothesis.

It has been necessary to touch briefly upon this prominent question since the assumption of a pituitary etiology for the genesis of diabetes insipidus has led to substitutive therapeutics with extract from the posterior (intermediary) pituitary lobe in subcutaneous injection or with the substance from the pituitary in its entirety, administered per os. Thus Umber (8) quotes a case in which the symptoms of disease completely disappeared after repeated injections with pituitrin during one day, and the patient remained free from symptoms for the fortnight during which he remained under observation. Another patient, whom Graul (9) had treated with pituitary injections on alternate days during a period of 16 days, afterwards came under supervision in hospital for the three following weeks, and then passed a quantity of urine not exceeding 2 litres per 24 hours.

It must, indeed, seem singular that a disease caused by an insufficiency of an endocrine gland should give place to stabilized

health, even after the supply of the missing secretion is discontinued. Such an occurrence seems rather to vitiate the theory. In practice, however, one must not deny the value of therapeutic means which have brought about such excellent results as the above-mentioned. Motzfeldt's (10) method, applied with great success, of giving the patient every evening fresh or dried pituitary bodies as a result of which the thirst and necessity of urination during the night were diminished, also speaks in favor of the proposed treatment.

Therefore, our decision at the Clinic to make an experiment on these lines should not seem surprising, and this all the more so as the symptoms of diabetes insipidus had shown no tendency to yield, in spite of the fact that the Wassermann reaction in accordance with the anti-syphilitic treatment had proved negative.

On March 13, our patient was given at an interval of three hours, at 8 and 11 a.m., a subcutaneous injection of 1.0 c.c. pituitrin. The urine passed during the ensuing 24 hours amounted to 5,075 c.c., as against 7,000 the preceding day and 6,000 and somewhat more the following days. Unfortunately, the injection was given before the extra dose of salt had been entirely eliminated, so that the quantity of urine passed during the 24 hours previous to the day of the experiment shows a higher figure than would otherwise have been the case. A distinct diminution of the diuresis can, however, be established, and this arresting power of pituitrin becomes still more evident from observations during the hours immediately after the injections (Table VIII). The urine was collected every hour, and during the two hours previous to the use of pituitrin amounted to 400 and 200 c.c. respectively, when it suddenly dropped to 40, and remained during the following hours, while the effect of the pituitrin still asserted itself, at 20 c.c. Afterwards a rise recommenced up to 300-400 c.c. The diminution of the diuresis was still more marked when compared with a control experiment, in which the separate portions of urine, for a period analogous with the time of the experiment, remained on a level between the limits of 220 and 425 c.c. (Table IX). No increased diuresis is observed, such as Kahlmeter had in one case noticed after the effect of the pituitrin had ceased, and I quote as an instance hereof a synoptic table (X)

of later date, when pituitrin was administered. For purposes of comparison it should be noticed that the urine during the night (7 p.m. to 7 a.m.) usually amounted to 1½-2 litres.

Simultaneously with the diminution of the urine the molecular concentration presents a rise. After a temporary decline of the freezing-point depression, as compared with the earlier

TABLE VIII.

Time	Quantity of Urine, C.C.	Freezing Point, °C.	N		NaCl		Sugar 0/00
			0/00	Gm.	0/00	Gm.	
6– 7 a.m.	400	–0.16	1.60	0.64	1.17	0.51	—
7– 8 "	220	–0.12	1.06	0.233	0.82	0.178	0.23
1.0 c.c. pituitrin							
8– 9 a.m.	40	–0.35	2.52	0.101	1.99	0.08	—
9–10 "	20	–0.87	5.82	0.116	4.68	0.094	—
10–11 "	20	–0.86	5.26	0.105	4.68	0.094	—
1.0 c.c. pituitrin							
11–12 noon	20	–0.74	5.74	0.115	3.51	0.07	1.9
12– 1 p.m.	18	.....	6.52	.....	....	.....	—
1– 2 "	28	–0.99	6.52	0.183	6.55	0.183	—
2– 3 "	305	–0.12	1.12	0.341	1.3	0.397	—
3– 4 "	445	–0.10	0.81	0.35	0.64	0.285	0.21

TABLE IX.

Test Experiment Time	Quantity of Urine, C.C.	Freezing Point, °C.	N		NaCl		Sugar 0/00
			0/00	Gm.	0/00	Gm.	
6– 7 a.m.	220	–0.14	1.04	0.229	0.59	0.13	—
7– 8 "	280	–0.12	0.87	0.24	0.53	0.15	0.23
8– 9 "	400	–0.09	0.87	0.35	0.53	0.21	—
9–10 "	320	–0.08	0.95	0.30	0.47	0.15	—
10–11 "	340	–0.10	0.84	0.29	0.53	0.19	—
11–12 "	240	–0.10	0.87	0.21	0.70	0.17	0.18
12– 1 p.m.	250	–0.13	0.92	0.23	0.82	0.21	—
1– 2 "	425	–0.11	0.74	0.31	0.53	0.23	—
2– 3 "	365	–0.11	0.87	0.32	0.59	0.22	—

morning urine, a large increase took place after the injection. While the test experiment with the different portions of urine presents values varying between -0.08° and -0.12°, the freezing-point depression has reached a maximum value of -0.99° at 2 p.m. (Table VIII).

With the increased total concentration the percentage of the NaCl and N secretion is augmented, but not in corresponding proportion as Norgaard found. A certain retention of these substances occurs.

A certain interest attaches to the observation that pituitrin causes an abnormal excretion of sugar, fixed on one occasion at 1.9 o/oo, and that is particularly remarkable when one considers that in normal individuals the subcutaneous injection of pituitrin as a rule has no such effect.

On three later occasions, commencing April 4 and 27 and May 4, the patient for a few days received pituitrin injections

TABLE X.

Time	27 April	28 April	29 April	4 May	5 May	6 May	7 May
	C.C.	C.C.	C.C.	C.C.	C.C.	C.C.	C.C.
8 a.m.	300	250	380	240	300	400	320
1.0 c.c. pituitrin							
9 a.m.	20	20	20	20	20	20	20
10 "	30	30	30	30	25	20	20
11 "	40	30	40	80	60	20	20
1.0 c.c. pituitrin							
12 noon	20	20	20	20	20	20	20
1 p.m.	20	20	20	20	20	20	20
2 "	20	20	20	20	20	20	20
3 "	20	20	20	20	20	20	100
4 "	20	40	20	20	20	20	200
5 "	30	40	30	20	20	20	50
6 "	60	240	150	100	100	120	50
7 "	60	100	200	100	150	120	40
Night Urine	1360	1870	1650	790	955	1280	990

in a similar way, the result being that the effect of the pituitrin in regard to the diminution of the diuresis was considerably more prominent than on the first occasion. The lowest quantity of urine per 24 hours on the respective occasions was 4,600, 2,000 and 1,300 c.c., corresponding to 6,000, 6,000 and 5,200 c.c. per 24 hours before the injection. When the injection of pituitrin had been discontinued, the urine showed some increase after the period beginning April 4, but both after the single experiment and after the two following periods the diuresis continued to be smaller than before the experiment.

In regard to the effect of the pituitrin upon NaCl and N in the daily quantity of urine, it is conspicuous that no stability

can be noticed. The first and third experiments (March and April 27) show no increased percentage of NaCl excretion, although this is found on the two other occasions. The total quantity of NaCl remains approximately unchanged during the first two periods of experiment, but shows an obvious decrease during those of later date.

Generally speaking, a percentile increase in the excretion is to be observed, but the total quantity of N per 24 hours is nevertheless lower than before the pituitrin injections.

The effects of the pituitrin on the patient with diabetes insipidus examined by me may perhaps be summed up thus: the diuresis always presents a diminution and the molecular concentration in the urine shows a rise parallel with this and approximately proportional to the diminished quantity of urine. Sodium chloride and nitrogen, to judge from their total amounts, are on the whole eliminated in smaller quantities, even on the occasions when there is a considerable increase per cent in their excretion. No constant effect can be established.

My own experiments in regard to the value of pituitrin in the treatment of the diabetes insipidus case in question have thus yielded not altogether favorable results. In view of the experience thus attained, and with the foregoing discussion in the background, the opinion can hardly be considered exaggerated that this method of treatment by no means involves any therapeutic attack upon the original causes of the disease. In spite of the apparently good results shown in the cases adduced by Umber and Graul, and more recently by Schnabel and Gerhard (11), the majority of cases in the extant literature of the subject have only a transitory "success" to show, and I am skeptical as to the advisability of adopting the use of pituitrin as a general method of treatment. This standpoint may, in my opinion, be defended by calling attention to the far from desirable diminution of the excretion of sodium chloride which may take place during the pituitrin treatment. If, on the other hand, as was the case with the patient examined by Norgaard, an increase in the absolute excretion of NaCl is the consequence of the pituitrin injections, this method of treatment is probably worth trying. But with Motzfeldt I propose as a symptomatic method of treatment the introduction towards night-time of

pituitary substance. By this means my patient secured an obvious subjective relief from the otherwise somewhat troublesome feeling of thirst and the need of urinating during the night.

There remains the dietetic treatment. In order to reduce the patient's feeling of thirst and to save him the frequent urination, which during the night is particularly disturbing, it has hitherto been the general therapeutic rule to reduce as far as possible the use of saline and protein foodstuffs. Of Swedish authors, af Klercker, for instance, says that in the symptomatic treatment of the disease "the arrangement of a suitable and as far as possible non-saline and non-protein diet must be the chief object," and Hedenius remarks that "the essential point in the treatment is to try as far as possible to lessen the secretory work of the kidneys by diminishing the supply of salt and reducing the supply of protein to a bare minimum.

It goes without saying that such a diet must after some time become monotonous. And not only so, but the addition of vegetables, which must be made in consequence of the reduction of sodium chloride, has a still more troublesome effect upon the patient, it being a well-known fact that a vegetarian diet brings an increased demand for salt. However, the experience gained by my experiments makes it *now possible*—at least in cases similar to the one analysed by me—*to vary the diet somewhat by the introduction of a more protein food,* and it may even be questioned whether it be not advisable in these cases to introduce from the very beginning of the treatment a larger quantity of protein, in order the more rapidly to deprive the patient of his reserve fund of sodium chloride.

SUMMARY

The principle of treating diabetes insipidus has been to limit sodium chloride and protein because it is assumed that secretory power for NaCl and N is limited. Critical examination of the literature and personal experience fails to substantiate this as generally true. In the dietetic treatment only the sodium chloride need ordinarily be reduced. In certain cases it appears that permanent improvement has been attained by the administration of pituitrin. Principally on theoretical grounds it appears unjustifiable to resort to it uncritically in every case. Pituitrin injections raise the concentration of the urine simul-

taneously with diminution of the quantity secreted, thereby restoring the kidneys to a partially normal state. But the concentration does not in every case rise in proportion to the diminution of quantity, resulting in a certain retention of NaCl. In such cases pituitrin should not be used and before it is employed the foregoing principle should be considered. An illustrative case is reported.

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A PSEUDOHERMAPHRITIC COCK

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The subject of this study was described as a hen that crowed and laid eggs but never brooded. Thinking that this might be a case of "masculismus" with altered endocrine function we secured the bird. It was a little larger than average, weighing 1950 gms. The plumage resembled closely that of a normal hen. It apparently was related to the race of Sebright Bantams. Like the cocks of this race, our animal had a thick and heavy comb—7 cm. long and 2.5 cm. wide. The wattles and ear appendages did not differ appreciably from those of a normal cock.

At necropsy the sub-peritoneal fat was found abundant. In front of the vertebral column, at the level of the genital glands, on the right side was seen an oval body, somewhat lobulated in appearance—2.75 cm. long and nearly 2 cm. wide. In form and color it resembled a testis, but its consistency was much firmer than that of a normal testis in this species.

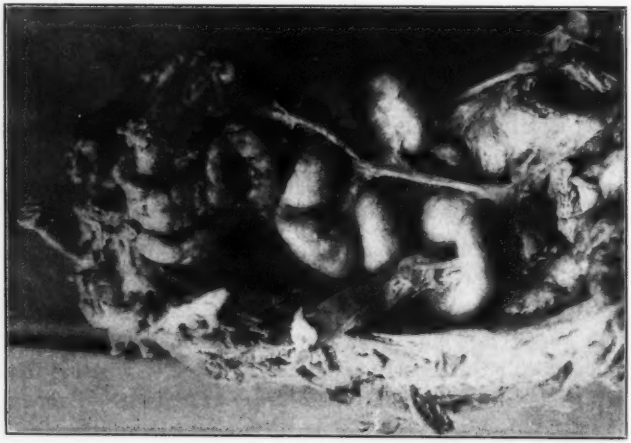
On the left side was a tri-lobed body, the right portion of which was 3 cm. long. This part was bounded by a horizontal portion, with a third part having nearly the same length. It was much lobulated and, in places, markedly granulated. In consistency, the body was as hard as cartilage and its color was bright yellow; that of the formation on the right side was grayish white. We believed the tri-lobed body to be a modified ovary, owing to the presence of a well developed oviduct similar to that of laying hens. But the consistency of the tri-lobed body was not that of the normal bird ovary and did not show any eggs.

There was a similar canal on the left side. Microscopic examination showed both to possess the characteristic structure of the oviduct in the laying hen. The accompanying photograph shows the genital glands and the excretory ducts of this bird.

The adrenals appeared microscopically and macroscopically normal.

The thymus was well developed, forming a complete band on the right side and a band more or less interrupted on the left. The thyroids were the size of a lentil. The liver appeared rich in fat, while the pancreas was rather reduced, especially in the region of the tail.

In the organ on the right side, the microscope disclosed in places the structure of the testis of a normal cock, with well developed seminiferous tubules and active spermatogenesis. In other parts was seen a structure characterized by fairly thick,



almost hyalin, connective tissue rings resembling those of testicular sclerosis in man. These rings are certainly derived by the hyperplasia of the peritubular connective tissue. The cells of the tubules were almost completely lost at these places. It was the dense connective tissue which gave to the organ the hard consistency mentioned.

In general, the interstitial gland was only slightly developed throughout the organ.

In the tri-lobed structure of the left side, which we took for an ovary, microscopic examination failed to reveal any ovarian

characteristics. In the microscopic study of the two structures, right and left, more than 3260 sections were examined, hence any ovarian tissue present would have been seen. The tri-lobed body resembled a testis more or less modified according to the region examined. Some regions possessed well developed seminiferous tubules showing spermatogenesis. In other regions was seen a slight degree of peritubular sclerosis. In places in both the right and left structures numerous foci of cellular infiltration having a lymphoid appearance were seen.

Certain regions, especially the connective tissue rings, were thick and almost hyalin, like those of the structure on the right side. In certain places, particularly where the sclerosed peritubular rings were the most noticeable, a well developed interstitial gland was observed, the cells of which were completely filled with lipoid granules. These were particularly noticeable in sections stained with Sudan-hematoxylin. Similar granules were observed in the cellular rests occasionally found in the interior of the sclerosed rings. In certain regions there were cords or masses of epithelial cells, more or less well circumscribed, but in which all evidence of spermatogenesis was absent.

Finally, in other regions the epithelial cells were more or less broken up by new connective tissue containing numerous cellular forms, including fibroblasts.

The surface of certain regions in the organ of the left side showed cystic formations of variable size, some of which occupied the greater part of a microscopic field (Zeiss ocular 4, objective A). These formations—which recall the retroperitoneal cysts observed in rare cases in man, and which seem to have genetic relations with the anlagen of the genital glands—contained an albuminous substance, staining as does the colloid of the thyroid, or the contents of the uriniferous tubules in albuminuria.

Nothing of particular interest was noted microscopically in the hypophysis, thymus, liver, spleen or pancreas.

SUMMARY

The case of a cock is described the testicles of which had been modified by a pathological process and which possessed two structures having the appearance of the oviducts in the laying

hen. (According to our observations there is a regression of the oviducts during brooding in connection with the endocrine modifications, which, according to our opinion, determine the brooding state.) Since no signs of ovarian tissue were found, the "oviducts" are difficult to account for. The endocrine organs other than the gonads appeared normal. The case is to be regarded as one of pseudohermaphroditism.

CLINICAL STUDY OF A PATIENT SUFFERING FROM INTENSE THIRST AND POLYURIA (DIABETES INSIPIDUS) AND PRESENTING X-RAY EVIDENCE OF MALIGNANT PROCESSES IN THE CRANIAL BONES, POSSIBLY LATE METASTASES OF MAMMARY CARCINOMA

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Recently there came under our observation a patient who had developed intense thirst and polyuria, which seemed to be associated with the appearance of malignant metastases in the bones of the skull. The case would seem to be of sufficient importance to put on record.

ANAMNESIS

The patient, who was brought to us for consultation by her family physician, was a woman of 58 years, the wife of a well-to-do business man.

She complained chiefly of excessive thirst, of very frequent urination, of weakness, of peculiar morning vomiting and of marked disability in the lower part of the back.

The family history was negative except that one sister had died of metastases of a cancer of the breast.

The patient herself had ordinarily been well except for chronic constipation. She had had four children and three miscarriages, and had passed the menopause at 43 with no remarkable symptoms. At 48 the left breast was removed by a competent surgeon because of a tumor, supposed to be a carcinoma.

The present illness had its beginning seven months before consultation. The patient noticed pain in the back and in various joints, especially the shoulders, knees and hips; but there was neither redness nor swelling and the pain in the various joints was inconstant and variable. The development of bilateral sciatic pain forced the patient to remain in bed for a short time.

Simultaneously with the development of these symptoms referable to the locomotor system, there appeared intense thirst and frequent urination. There was also marked anorexia, slight nausea and some morning vomiting of mucoid froth.

Gradually the sciatica and joint pains grew less and the patient was able to get about, though she still suffered from marked disability of the back. The gastric symptoms, however, continued as did

the polydipsia and the polyuria. At times a little clotted blood appeared in the throat, apparently coming from the posterior nares. There were two attacks of diffuse erythema of the legs, each attack lasting a day or two, to be followed by scaling. Twice there was transient diplopia while motoring. There was weakness and much loss of weight. The patient stated that, at times, she voided more than a gallon of urine in twenty-four hours. There was some itching of the skin. There was no headache. All the teeth had been removed four months before consultation.

STATUS PRAESENS

Examination at the time of our consultation showed a pale, feeble woman, still well nourished despite much recent loss of weight. Pupils and eye muscles showed no abnormalities. Ears and hearing were normal. The tonsils were small, slightly irregular, and showed a few occluded crypts. There was no thyroid struma. A few small retrocervical glands could be felt, but otherwise there was no glandular enlargement. The scar of the left breast operation was in excellent condition. The lungs were negative. The heart was normal. The pulse rate was 96. The blood pressure measured 120 to 130 systolic and 80 diastolic. There was no appreciable thickening of the peripheral blood vessels. There was a little tendency to round back, and the movements of the whole spine were very stiffly carried out. The most discomfort appeared to be localized in the lumbar region. The abdomen showed nothing remarkable. The deep reflexes and abdominal reflexes were normal. The sign of Babinski was negative. Neither sciatic region was tender and Kernig's maneuver caused no unusual discomfort.

LABORATORY REPORTS

During the weeks just preceding consultation, numerous careful, special examinations had been made in the hope of throwing more light upon the condition. The main results of these tests follow.

Blood Examination: Red blood cells, 3,752,000; hemoglobin, 75 per cent; white blood cells, 5,800; blood Wassermann, negative; blood sugar, 121 mg. per cent; blood nitrogen, 30.5 mg. per cent; blood creatinin, 1.5 mg. per cent.

Urine Examination: Sp. gr., 1,002; acid; no albumin; no sugar; in the sediment no casts, but occasional pus cells were found. Tests of the urine were made repeatedly with negative results, except for persistently low specific gravity (usually about 1,002). The amounts of urine were always large for each twenty-four hours.

Examination of Stomach Contents: Free HCl, 12 acidity per cent; total acid, 40 acidity per cent; lactic acid, absent. The stomach contents were examined on several different occasions; once small blood clots were present in the stomach washings.

Feces: Occult blood was found in the stool on one occasion.

Cerebrospinal Fluid: Clear; 5 cells; Wassermann reaction, negative; tests for globulin, negative.

X-RAY STUDIES

Five months before our examination evidence of infectious arthritis of the thoracic and lumbar spine was visible in roentgenograms, but nothing further could be made out. Three weeks before consultation various long bones had been studied by means of the x-ray, on suspicion of a possible malignant condition, but nothing was found, and the arthritic changes in the spine were regarded as sufficient explanation of the symptoms in the back. The gastrointestinal tract had also been carefully studied roentgenologically, but no evidence of any lesion in the stomach or intestines beyond adhesions in the right upper quadrant of the abdomen was obtained.

NOSE AND THROAT EXAMINATION

An ulcer had been found on the left aspect of the nasal septum. It was believed that this might explain the occasional appearance of blood in the nasopharynx, the blood clots once found in the stomach content, and, perhaps, also the occult blood in the feces.

SUMMARY

On summing up the situation, the principal features were as follows:

1. Loss of weight and strength.
2. Gastric symptoms, including nausea, morning vomiting and anorexia.
3. Polyuria and polydipsia.
4. Disability of the spine.

Of these, the fourth was easily explicable, apparently, on the basis of x-ray findings of infectious arthritis of the spine. No local cause had been found for the gastric symptoms. The loss of weight and strength and the general appearance of the patient made one fearful of a malignant process somewhere in the body, but none had been revealed. The urinary studies, blood findings and blood pressure were all rather against the polyuria being a manifestation of chronic nephritis, and there was nothing to suggest that it was of hysterical origin.

EFFECT OF INJECTIONS OF PITUITRIN

It seemed best to investigate next the effects of pituitrin upon the polyuria. The amount of urine excreted during the twenty-four hours preceding was found to be 3,000 cc. One milligram of pitui-

trin was injected, hypodermically, twice a day for two days. During the first twenty-four hours after injection the urinary output was 2,500 cc., the amount of water ingested 2,000 cc. During the second twenty-four hours the urinary output was 2,000 cc., and the amount of water ingested was the same. The nausea was definitely less and the nocturia was reduced to two urinations the first night of the test and to one the second night.

EYES AND EYE GROUNDS

The eye grounds were carefully examined and found to be perfectly healthy. Central vision was good. The fields of vision, however, showed marked contraction for form and for colors. The ophthalmologist's report reads: "Without knowing anything of the general complaint of the patient, the markedly contracted fields point strongly toward hysteria."

X-RAY FINDINGS IN THE SKULL

X-ray studies of the skull showed normal paranasal sinuses, including the sphenoidal sinus. The sella turcica was of the flat, open type with no sign of any destruction of the base, or of the clinoid processes. Scattered through the cranial bones, particularly in the parietal and frontal regions, there were numerous rarefied areas of bone destruction, showing no evidence of new bone formation; the process in the bones was apparently invasive in character, in every way resembling the changes in malignancy.

COURSE AND TERMINATION

The patient's condition changed but little while under our observation. The cutaneous itching was controlled by a mild carbolic ointment. The polyuria became less marked and required no further use of pituitrin. The gastric symptoms persisted. About two weeks after our examination the patient gradually became dull, then comatose, and died on the third day of the coma, according to the report of the family physician, with evidence of increased intracranial pressure.

DISCUSSION OF SPECIAL FEATURES

The case presents a number of interesting possibilities and problems.

(1) In the first place, what was the origin of the apparently malignant processes in the bones of the skull? The lesions were multiple and certainly metastatic in origin. Repeated careful search was made for a primary, malignant process in the body; none was found, though this does not, of course, exclude the existence of such a lesion. Can we connect the sup-

posed left breast cancer, removed ten years earlier, with these metastases? The possibility must, of course, be kept in mind. Ordinarily, we feel pretty safe, in a cancer case, if the patient is entirely well three years after operation; and after five years, one is accustomed to look upon the cancer as cured. Crouzon and others, however, have reported late multiple metastases in the brain in two cases after removal of the breast for cancer. In one of these, the metastases occurred eighteen years after, and, in the other, twenty years after operation. The interval in our case was ten years.

We know, also, that carcinoma of the breast is the commonest cause of bone metastases in women, just as carcinoma of the prostate is the commonest cause in men. The order of frequency of the bones showing such metastases in women is as follows: Ribs, thoracic spine, lumbar spine, ilia, femur, skull and humerus. In this connection, it may be said that we were a little suspicious of a malignant process in the lumbar spine, though at the time of the x-ray examination there was no visible evidence of it.

(2) It would seem highly probable that the intense thirst and the polyuria exhibited by the patient should be viewed as evidence of the existence of a mild diabetes insipidus. The patient said that she had frequently voided more than a gallon of urine in twenty-four hours, though even this is, of course, a small amount in comparison with the quantities passed in many of the reported cases of diabetes insipidus. Many such cases have certainly suffered from diseases of the pituitary gland or of the floor of the third ventricle in its neighborhood. In our case, it seems reasonable to infer the presence of a metastatic growth in the region of the pituitary or of the floor of the third ventricle. Negative x-ray findings in the region of the sella would be expected, unless the growth had been of sufficiently long standing to bring about bone destruction. Many of the reported cases of diabetes insipidus have shown tumors in the region of the pituitary when examined post mortem.

(3) Can our case be related to the remarkable condition recently reported by Christian? His case was an exceedingly interesting one, that of a child of five years presenting the symptom complex of: (1) Extensive defects in the bones of

the skull; (2) exophthalmos, and (3) diabetes insipidus. There were also less marked defects in the pelvic bones. Christian cites two other cases showing similar bony defects in the skull; one was that of a young boy with dystrophia adiposogenitalis and exophthalmos; the other that of a girl of four years with exophthalmos and diabetes insipidus. In the latter case, the x-ray revealed a defect in the right ilium and a spindle-like thickening in the upper part of the right femur. These two cases cited by Christian had been reported by Schüller, and in both instances, basilar intracranial tumors presumably existed; basilar tumors would not account, however, for the areas of bone destruction seen in the cranium in both cases nor for the additional defects in the pelvis and femur seen in one of the cases, particularly since the physical condition of both children was too good to allow one to accept the theory of the existence of metastases. Christian believes that the bony defects in all three cases are to be explained by changes in the function of the pituitary gland.

It does not seem probable that our case falls in the group just cited, since the x-rays in our patient revealed irregular-shaped, scattered areas, suggestive of an invasive, destructive process, whereas in the three cases reviewed by Christian, the bony margins of the defects were very sharply and clearly defined.

CONCLUSIONS

In retrospect, we should be inclined to regard the case reported here as one of multiple, malignant metastases in the bones of the skull, at the base of the brain, and, possibly, also in the lumbar spine. It is probable that the involvement of the base of the brain affected the mechanism regulating water metabolism, so that symptoms of mild diabetes insipidus developed. The origin of the metastases is uncertain, but it is quite possible that they were secondary to the breast cancer removed ten years before.

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CHANGES PRODUCED IN THE LARVAL BRAIN OF RANA PIPIENS BY THYROID FEEDING

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LAWRENCE

During the past decade, numerous investigations have been carried on, which have demonstrated that a very definite relationship exists between the thyroid gland and body growth. By the pioneer work of Gudernatsch in the field of thyroid feeding of tadpole larvae, a beginning was made which has since been so extended by numerous investigators that the field covered has grown most extensive in scope. Allen, in connection with his experiments on thyroid removal, has shown that the brain of thyroidless tadpoles does not proceed to maturity, but retains the early larval form. It has been shown by Larson and Rogers, that there is a definite relationship existing between the thyroid gland and the anterior lobe of the hypophysis, since normal development and growth does not occur in the absence of either. Felix Adler and P. E. Smith have done valuable work along the same line, while Swingle has shown that thyroid feeding has no influence on the development of the gonads of tadpole larvae. However, thus far there seem to be on record few data concerning the effect of thyroid feeding or hyperthyroidism on the general structure of the brain.

Early in the fall of 1920, the writer began a series of thyroid feeding experiments for the purpose of ascertaining, if possible, the effect of hyperthyroidism on the general brain structure of the developing larvae of Rana pipiens. Measured from the tip of the snout to the cloacal opening, the tadpoles averaged about 8 mm. in body length at the beginning of the experiment. The material used for food was composed of one part of thyroid powder prepared by Armour & Co., two parts of dried clover leaves, and eight parts of flour, thoroughly mixed into a paste and dried in thin sheets. The control food was made in the same way, except for the absence of thyroid powder, for which powdered egg yolk was substituted to make up the deficiency in protein.

The tadpoles were carefully matched in size, half of each size being used as controls. The food was given in small quantities twice a day and water changed in the bowls at the same time. The feeding continued as long as there were any thyroid-fed tadpoles alive in the various lots, and whenever a thyroid-fed tadpole died, a control of the same lot was taken out and both preserved in formalin for dissection. The brain was dissected out under a binocular microscope, by means of very fine pointed forceps and needle scalpel. Body measurements were made as above indicated, with a small caliper and millimeter rule. Brain measurements were made with an eye piece micrometer.

As has been previously described by Gudernatsch, Swingle and others, no external changes take place for four or five days, then a very remarkable differentiation begins, which gradually increases with feeding. As Swingle (1918) has described these external changes fully, it will be unnecessary to discuss them further than to say that, by exceeding care, a few tadpoles were kept on a thyroid diet for 40 to 60 days, thus becoming almost completely metamorphosed.

In the spring of 1921, two more lots were started, one averaging 4 mm. in body length and the other averaging around 15 to 18 mm. These lots of nearly 50 each, were fed in the same way as those of the previous fall and with essentially the same results. The last series of feeding experiments was made during the summer of 1921 and in this work the tadpoles were matched very carefully as to size and the thyroid feeding pushed fairly rapidly. These tadpoles averaged from 12 to 15 mm. body length.

RESULTS

External Body Changes: The general external changes were exactly the same as those found by other workers, hence it is unnecessary to describe them in detail. As the results in the various lots of tadpoles were compared, however, a few marked differences were seen. For example, the first lot, consisting of tadpoles of 8 or 9 mm. body length, showed themselves able to stand the thyroid feeding much better than those averaging only 4 to 6 mm., and they were able to progress much further than the latter toward complete metamorphosis before death. It was also shown that the tadpoles fed in the late fall were more resistant to the toxic action of the thyroid hormone than those

fed in the early summer, since the average length of life of the tadpoles fed thyroid in the winter was 26 days, while the average in the summer was only 8 days. Those fed in the summer also had a great deal higher rate of metamorphosis than those fed in the winter, for, although the average length of life of the two lots was markedly different, the extent of metamorphosis was very much the same, as shown by the external indices of body development.

This, then, seems to indicate two things: the seasonal factor affects the amount of thyroid a tadpole may consume before yielding to its toxic effect; second, the length of life of the thyroid-fed tadpole varies directly as the amount of body tissue at the outset of the experiment. The seasonal effect may be due to the accelerated metabolism during the summer months and the greatly increased glandular activity, all of which would result in an increased susceptibility to thyroid feeding. The relation to body size at the beginning of the experiment may be due to the fact that the increased nitrogen metabolism brought about by the thyroid hormone is more easily withstood in the case of the larger and older tadpoles. Perhaps reserve materials may be stored in the larger tadpole, which can be utilized in the formation of new features of metamorphosis. Certain it is, the more body substance present, the further the tadpole proceeds toward complete metamorphosis before death.

Brain Changes: Just as there is a difference in the extent of external change caused by the two factors of season and body size, so in the case of the brain structures, the extent of metamorphosis depends somewhat on the length of time the tadpoles are able to live and feed on thyroid, and on the season of the year. However, there is evident a uniformity of change, which, although more marked in those fed longest, is nevertheless present throughout the series.

Beginning at the cranial portion of the brain, it is found that the cerebral hemispheres in the average case assume a more blunt appearance and lengthen out into a form very similar to that found in the adult frog. The pineal body, instead of standing out clearly defined between the caudal curves of the two lobes, is almost completely imbedded in the tissues of the diencephalon. The diencephalon itself seems to be crowded in between the optic lobes and cerebral hemispheres in a very pecu-

liar fashion and is much shortened antero-posteriorly and broadened and extended laterally. The shortening, as shown by data, is 40.65 per cent, while the broadening amounts to 19.78 per cent.

The optic lobes, especially in those specimens nearly meta-

Tadpole Number	Body Length	Brain Length	Width at Cer. Hem.	Length of Dienceph.	Width of Dienceph.	Length of Fossa Rh.	Width of Fossa Rh.	Length of Ant. Lobe	Width of Ant. Lobe	
C1	12.0	3.98	1.69	.96	1.44	1.67	.70	.357	.324	
E2	12.0	3.74	1.49	.41	1.62	1.66	.20	.239	.324	
C3	12.8	3.62	1.62	.76	1.25	1.67	.60	.297	.389	
E4	12.5	3.74	1.29	.42	1.85	1.44	.30	.238	.320	
C5	11.6	3.12	1.35	.68	1.06	1.44	.51	.328	.292	
E6	10.0	3.13	1.35	.35	1.31	1.33	.36	.296	.324	
C7	16.0	4.11	1.82	1.01	1.50	2.00	.77	.357	.390	
E8	14.5	4.29	1.67	.47	1.91	1.10	.40	.327	.385	
C9	15.0	3.68	1.69	.82	1.53	1.66	.77	.356	.390	
E10	13.0	3.68	1.60	.29	1.87			.356	.356	
C11	18.0	4.29	1.95	1.01	1.77	2.21	.81	.356	.485	
E12	16.0	4.60	1.80	.56	1.86	1.77	1.10	.354	.452	
C13	17.0	4.23	1.82	.96	1.62	1.94	.97	.327	.389	
E14	13.8	4.29	1.80	.58	1.74	1.99	.40	.350	.325	
C15	17.0	4.41	1.79	1.01	1.62	1.77	.91	.386	.480	
E16	15.0	4.29	1.61	.58	1.74	1.79	.50	.310	.422	
C17	16.0	3.74	1.69	.82	1.55	1.72	.71	.302	.324	
E18	13.5	4.05	1.61	.35	1.74	1.77	.40	.297	.321	
C19	16.3	3.80	1.62	.86	1.31	1.94	.81	.297	.324	
E20	13.0	3.64	1.35	.35	1.62	1.39	.40	.297	.324	
C21	15.5	3.68	1.62	.84	1.37	1.83	.85	.290	.320	
E22	13.5	3.80	1.67	.47	1.74			.324	.385	
C23	10.8	2.76	1.29	.64	.93	1.27	.64	.327	.324	
E24	8.5	2.70	1.29	.29	1.31	1.27	.30	.297	.292	
C25	15.4	3.86	1.51	.82	1.37	1.66	.71	.327	.356	
E26	14.0	4.11	1.42	.37	1.56	1.38	.71	.290	.385	
C27	9.0	2.01	1.26	.55	1.00	1.33	.50	.297	.260	
E28	6.6	1.65	1.01	.29	.93	1.10	.55	.155	.164	
	−2.0	+.04	−.083	−.25	+.22	−.22	−.14	−.07	−.04	Average Deviation
		1.76			19.78					Percentage Increase
	13.89		6.50	40.65		14.20	38.40	12.50	6.7	Percentage Decrease

Data compiled from lot fed during summer. C—Represents control tadpoles and E—epresents thyroid fed tadpoles. All measurements given in millimeters.

morphosed by the thyroid feeding, appear very similar to those of the brain of an adult frog. The globular appearance of the early tadpole stages has entirely disappeared and a more triangular shape assumed as is shown in accompanying diagrams. The

lateral surfaces of the lobes are flattened perceptibly and sometimes a slight depression is formed on the ventral lateral surface (Fig. B3), due to the pressure of the forming auditory capsule.

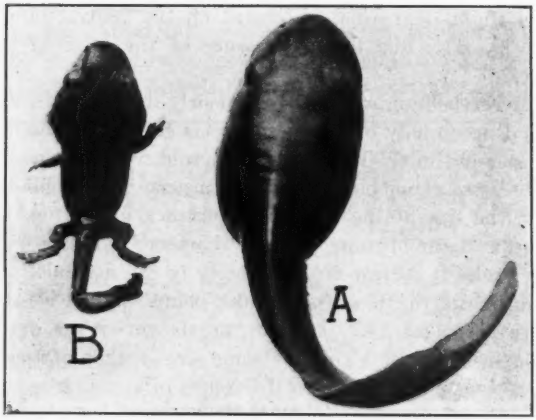
The cerebellum, which is very poorly developed in the adult frog and necessarily offers poor criteria for study, shows only a slight increase in thickness in the thyroid-fed tadpoles.

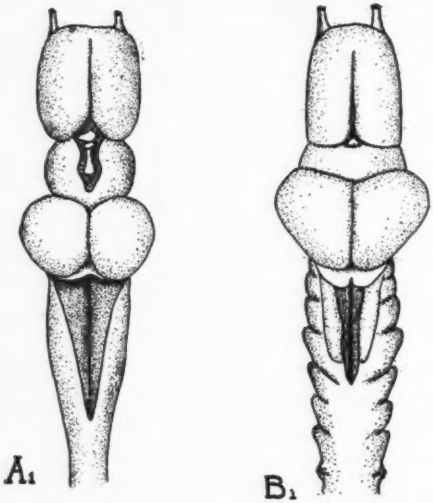
The fossa rhomboidalis presents a very remarkable differentiation; the lips of the ventricle are much closer together and the length of the opening is much shortened. This is especially striking since it corresponds so closely to the normal changes of metamorphosis, the decrease in width being 38.4 per cent and the decrease in length 14.2 per cent, as shown by the data. The medulla seems to be about the same size as that of the control tadpole, with, however, a vast difference in appearance. Instead of a smooth, even surface around the margin of the part, the medulla is broken on its surface into small furrows or ridges, which extend a considerable distance down the spinal cord. By careful dissection, it is shown that these ridges are due to the force exerted on the hind brain and medulla by the forming neural arches of the vertebrae. The probable explanation seems to be that while the average body length of the thyroid-fed tadpole is 13.89 per cent less than that of the control, the brain length is 1.76 per cent greater. We thus have two diametrically opposed factors; insufficient room is left between the developing neural arches for the expansion of the brain structure and pressure is brought to bear on the medulla, which results in the production of furrows or ridges.

On the ventral side, the same changes as indicated above are evident, with the addition of changes in the hypophysis and infundibulum, the infundibulum being slightly broadened laterally shortened antero-posteriorly. The posterior and intermediate lobes of the hypophysis are not noticeably changed, but the anterior lobe shows a decided decrease in size, as is indicated by the data. Only a cursory examination of the intermediate and posterior lobes was made, however.

DISCUSSION OF RESULTS

Without question, the majority of the changes brought about in the brain of the developing tadpole by thyroid feeding are those commonly seen during normal metamorphosis of a tadpole



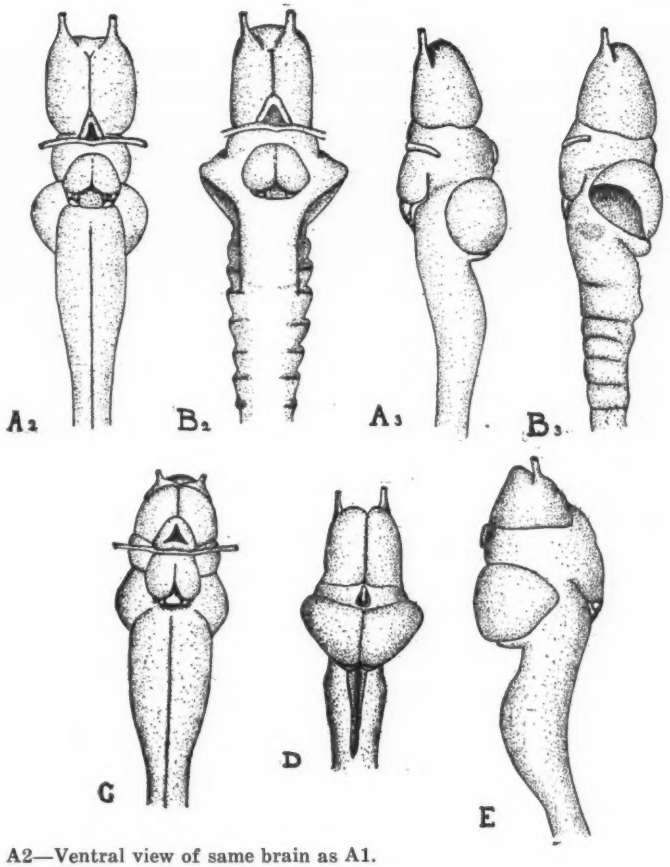


A —Control tadpole, fed 40 days. Body length 17.8 mm.

B —Thyroid fed tadpole, fed 40 days. Body length 17 mm.

A1—Control tadpole brain, dorsal view. Taken from tadpole A.

B1—Thyroid fed tadpole brain, dorsal view. Taken from tadpole B.



A2—Ventral view of same brain as A1.
B2—Ventral view of same brain as B1.
A3—Lateral view of same brain as A1.
B3—Lateral view of same brain as B1.
C —Lateral view of thyroid fed tadpole brain. Taken from 8 mm. tadpole fed in early spring. Fed 17 days.
D —Dorsal view of thyroid fed tadpole brain. Taken from 12 mm. tadpole fed in the early winter.
E —Lateral view of thyroid fed brain. Fed 18 days. Note the bulged appearance of the medulla in the region of the fourth ventricle. This was sometimes so marked that it could be seen from the outside with the naked eye. It is due to the closing together of the lips of the fourth ventricle.

larva. This is especially true of the closing of the fossa rhomboidalis, the changed appearance of the cerebral hemispheres and optic lobes and the shortening of the diencephalon. These facts show that thyroid feeding greatly accelerates the development of the brain, causing it to assume adult characteristics in a comparatively short time, as is clearly shown, for example, by the shortening of the diencephalon, which averages 40.65 per cent and the decrease in the width of opening of the fossa rhomboidalis, which averages 38.4 per cent in tadpoles fed only 7 to 11 days.

The abnormal appearance of several portions of the brain appears to be due to the various rates of growth in the body of the tadpole. Referring to the data, it is seen that the body length decreases under thyroid feeding while the brain length increases. From some standpoints, it is most remarkable that while the body as a whole is steadily falling behind in size, the brain is increasing. However, in the light of the numerous other changes produced when the rate of metamorphosis is accelerated by the thyroid feeding, it may be no more striking than the very rapid growth of the fore and hind limbs or any of the numerous other changes leading to maturity.

As to the anterior lobe of the hypophysis, there seems to be some question on the interpretation of results. Rogers (1918) shows that the anterior lobe of thyroidless tadpoles increases in size considerably beyond the normal. He also makes the statement that the anterior lobe of his controls shows an increase in size, corresponding to the body development of the tadpole. This seems to be the case from his data sheet; however, he made no very accurate study of these facts and obtained his results from but a few specimens. The most important question arising is that regarding the change in size of the anterior lobe during normal metamorphosis. If a decrease in size is common, then hyperthyroidism does nothing more than bring about the normal change of metamorphosis. However, in view of the proven relationship existing between the anterior lobe of the hypophysis and the thyroid gland, it may be that the presence of an excess of thyroid hormone has lessened the necessity for the complete function of the anterior lobe and a slight degree of atrophy has resulted.

SUMMARY

Armour's thyroid powder, mixed with powdered clover leaves and flour, was fed twice a day to a large series of frog tadpoles. Experimental and control tadpoles were carefully matched in size. The thyroid accelerated metamorphoses and also exerted a toxic effect, greatest in the summer, less in the spring and least in the autumn. The larger tadpoles survived longer and metamorphosed to greater extent than the smaller. In all parts of the brain of the thyroid fed tadpoles, adult characteristics were evident. The body length decreased 15.89% while the brain length increased 1.76%; the fossa rhomboidalis was much shortened; the cerebral hemispheres lost their globular form; the anterior lobe of the hypophysis was diminished in size; and other changes closely resembling those of normal metamorphosis were seen. Many striking abnormalities were produced in various parts of the brain, caused by pressure from surrounding structures. These were due to abnormal differential rates of growth.

In conclusion, I wish to acknowledge my indebtedness for the very great assistance and encouragement of Dr. B. M. Allen of Kansas University, at whose suggestion this problem was undertaken.

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SOME FACTORS WHICH MODIFY THE EPINEPHRINE REACTION

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Oliver and Schafer (1) found that extracts of the suprarenal glands when injected intravenously produced a marked rise in blood pressure. Elliott (2) studied the vascular response to epinephrine in great detail and found that the rise in blood pressure following the injection of epinephrine into an animal with the central nervous system destroyed was, within certain limits, directly proportional to the amount injected. Investigations carried out by numerous workers demonstrated that the seat of action of epinephrine was chiefly, at any rate, the nerve endings of the sympathetic system, and that the effect of epinephrine was synonymous with stimulation of the sympathetic nerve supply. The point of action of epinephine was therefore considered to be entirely peripheral. The effect of stimulation of the sympathetic nerve supply to any structure being known, the effect of epinephrine on any organ could be correctly predicted.

That epinephine, in addition to its well defined peripheral action, has a central action as well was suggested by the experiments of S. J. Meltzer and C. Meltzer (3). They found that the intravenous injection of epinephrine caused definite vasoconstriction in the vessels of a rabbit's ear, but this constriction was followed immediately by dilation exceeding that which existed before the injection. Langley (4) obtained similar results in the case of the submaxillary gland while Lewandowsky (5) found that the rise in systemic blood pressure in cats following the administration of epinephrine was frequently followed by a fall below the original level.

Moore and Purinton (6) first demonstrated that the vascular response to very minute amounts of epinephrine was a definite fall in blood pressure, and this observation has been frequently confirmed by various workers in recent years.

Dale found that the pressor response to a moderately strong dose of epinephrine was converted into a pure depressor effect if ergotoxin were administered between the epinephrine injections. He concluded that there are two sets of vasomotor fibres in the sympathetic—constrictors and dilators—the effect of ergotoxin being paralysis of the vaso-constrictor nerve ending. Epinephrine administration after ergotoxin caused a pure fall due to peripheral action on the vaso-dilator nerve endings.

Hoskins and McClure (8), working with pure "adrenalin" confirmed the earlier results of Moore and Purinton. They concluded that, as the effect of small doses of adrenalin was to cause a fall in blood pressure, the suprarenals do not ordinarily produce sufficient secretion to maintain any pressor influence.

Cannon and Lyman (9) found, after ligation of the coeliac axis, the superior and inferior mesenteric and the renal arteries that stimulation of the splanchnic caused a sheer fall in blood pressure. This they attributed to liberation of a small amount of epinephrine into the circulation.

These observers showed also that considerable modification of the vascular response to epinephrine could be produced by varying the rate of injection. A certain dose given very slowly might cause a pure fall in blood pressure, while the same dose injected quickly might be followed by a rise in blood pressure succeeded by a slight fall with return to normal shortly thereafter, or else by a pure rise with no successive fall. These authors also found that the blood pressure level previous to the administration of epinephrine was an important factor in determining the type of response to the drug. Thus they found that a dose of epinephrine which at first caused a pure fall in blood pressure, caused a rise only after the blood pressure had been lowered by pithing. They concluded that the depressor effect of epinephrine was not due either to central action or to stimulation of supposed vaso-dilator endings of the sympathetic but to the condition of the muscle of the vessel wall.

They held that vaso-dilatation resulted from epinephrine action when the muscle was tonically shortened, vaso-constriction when relaxed. Hartman (10) later found that effect of small doses of epinephrine given by intravenous injection was dilatation of the limb vessels and constriction of those in the

splanchnic area. Hoskin, Gunning and Berry (11) showed that small doses of epinephrine produced constriction in the vessels of the cutaneous area and dilatation of the vessels of the limb muscles. Hartman and Fraser (12) obtained dilatation in vessels of the splanchnic area and of the limb muscles by central action of epinephrine. They attributed this result to direct stimulation of vaso-dilator cells, but they admit that dilatation may result by peripheral action as well. Gruber (13) failed to obtain vaso-dilatation in limb vessels the nerves to which had been severed. He attributed this result to loss of tonicity of the vessel walls, and is of the opinion that small doses of epinephrine cause dilatation by direct peripheral action.

Hartman and Fraser (12) also demonstrated that the dilator response of the limb vessels to adrenalin was effected by temperature. Thus they found that in a limb which had ceased dilating from artificial heat, the usual dose of adrenalin injected into the general circulation caused an increase in volume of the organ where previously the same dose of adrenalin produced either no effect or else constriction of the same.

It is quite evident in the light of the experiments above referred to that the response to the administration of epinephrine as judged by the change observed to take place in systemic blood pressure is no indication of the exact nature of what is occurring. It is rather the sum total of vascular changes in various parts. Either constriction or dilatation of vessels may be the predominating effect, depending very largely upon the dosage employed. Also constriction may result in one area and pure dilatation in another, while constriction followed by dilatation in any area is also a possibility.

Collip (14) has recently demonstrated new methods of producing reversal of the effect of small doses of epinephrine. Thus he found that a dose of epinephrine which causes a fall in systemic blood pressure can be converted into a pure rise, or into a slight rise followed by a slight fall, or else the fall will be greatly decreased by the injection of a variety of tissue extracts such as those prepared from heart, spleen, thyroid gland, suprarenal and pituitary bodies. This reversal or antagonism of the depressor action of small doses of adrenalin by tissue extract is of short duration only, the depressor response returning within a few minutes after the administration

of the tissue extract. It was found that similar reversal of the depressor action could be brought about by increasing the depth of anaesthesia. Also on occasion the response of the systemic blood pressure to a definite dose of epinephrine can be altered by previous administration of sodium carbonate or acid phosphate; sodium carbonate tends to increase the pressor effect of epinephrine while acid phosphate tends to decrease it.

Snyder and Andrus (15) obtained reversal of the effect of epinephrine on the isolated heart of the terrapin due to alteration of the hydrogen ion concentration of the perfusate. Snyder and Campbell (16) have observed reversal of the constrictor effect of epinephrine on the perfused vessels of a frog following increase in the hydrogen ion concentration of the perfusate while the constrictor effect was increased by a decrease in the hydrogen ion concentration.

The isolated uterus of certain animals is always inhibited by adrenalin when applied in very small amounts. Collip (17) has shown that this inhibition reaction to epinephrine is antagonized by small amounts of tissue extract. As the antagonism of the epinephrine reaction on certain isolated uteri by certain tissue extracts is very definitely a peripheral effect, it is quite possible that the antagonism or reversal of the depressor action of small doses of epinephrine on the systemic blood pressure by tissue extracts or by increasing degrees of anaesthesia is due to changes brought about in the periphery. The writer inclines to the view of Dale (7) that vaso-dilator as well as vaso-constrictor nerve endings are stimulated by epinephrine. The dilator endings are probably depressed by some constituent or constituents of tissue extracts with the result that the systemic blood pressure response to a small dose of epinephrine is definitely altered as above indicated. The fact that a dose of epinephrine which will produce a pure fall in blood pressure in an animal under very light anaesthesia will product a rise or a rise and slight fall when the anaesthetic is increased may be explained on the assumption that the vaso-dilator endings are more readily depressed by the anaesthetic than are the constrictors. However, sufficient data have not as yet been obtained to enable one to explain in any definite manner just how these reversals of vascular reactions to epinephrine are produced.

The cardiac response alone, for example, may be so altered under varied conditions as to play a large part in bringing about the observed results.

That vaso-dilatation may be associated with central action of epinephrine is suggested by the demonstration by McGuigan (18) that the response of the systemic blood pressure to a definite dose of epinephrine is increased following the administration of just sufficient nicotine to block central impulses along sympathetic pathways.

While the depressor action of a small dose of epinephrine may be completely reversed by increasing the depth of anaesthesia, it is also true that the pressor response to a large dose of epinephrine is decreased by anaesthesia.* This is due as McGuigan (18) points out to decreased irritability of the vaso-constrictor nerve endings, due to the increasing concentration of the anaesthetic in the blood stream.

McGuigan (18) has shown that haemorrhage causes an augmentation of the pressor response to adrenalin. He has interpreted this effect as indicating an increased irritability of the sympathetic vaso-constrictor nerve endings in the vessel walls as a result of haemorrhage.

The synergistic action of cocaine and epinephrine is still another example of the modification of the epinephrine reaction. This was first demonstrated by Frölich and Loewi (19). Recent experiments by Heinekamp (20) demonstrate a synergistic action between morphine and epinephrine as regards their central action on medullary centres.

It is now recognized as a result of the experiments of Levy (21) that the administration of epinephrine during chloroform anaesthesia is not without danger. He found that, if the animal were under light chloroform anaesthesia at the time of administration of the epinephrine, but had previously been deeply anaesthesised, the heart tended to go into fibrilation.

The vascular response of an intact animal to epinephrine administration may be considerably modified by varying the mode of injection. Thus a dose of epinephrine which calls forth a decided pressor response when injected intravenously if given subcutaneously, may have little or no effect on the blood pressure. Becht (22) has shown that installation of epinephrine

* Unpublished results of Groot and Albrecht kindly furnished by Professor Hugh McGuigan.

into the spinal canal produces a slight fall in blood pressure or else no effect. If, however, blood stained fluid exudes from the puncture needle prior to the injection a rise in blood pressure is frequently obtained. Variations in the response to epinephrine such as the above are probably related to the rate at which the active principle is introduced into the general circulation.

SUMMARY

A number of factors, which have been shown by various writers to produce a modification of the epinephrine reaction have been outlined.

The fact that very small doses of epinephrine cause a fall in blood pressure and not a rise has been emphasized.

Epinephrine may cause vaso-dilation in one area and vaso-constriction in another at the same time (Hartman and Fraser; Hoskins, Gunning and Berry).

A reversal of the depressor action of epinephrine may be accomplished by lowering the blood pressure level (Cannon and Lyman).

The pressor response of epinephrine is reversed by ergotoxin (Dale).

The reversal of the depressor action of epinephrine may be brought about by injection of tissue extract or by increasing the depth of anaesthesia (Collip).

Changes in hydrogen ion concentration may affect epinephrine response (Snyder, Campbell and Andrus; Collip).

The pressor response to epinephrine is decreased by anaesthesia (McGuigan).

The pressor response to epinephrine is increased following haemorrhage (McGuigan).

The mode of administration effects greatly the response to epinephrine.

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Book Reviews

La Cure de Bouchardat et la Traitement du Diabete Sucre (bouchardat's treatment of diabetes mellitus), by Prof. F. Rathery, Paris, 1920. Librairie Felix Alcan, 272 p.

This exceedingly practical book first describes the old treatment of diabetes by Bouchardat. This is done in such an entertaining way that the book reads like a novel. It is remarkable that some principles earlier stated by Bouchardat are of fundamental importance in modern treatment. Thus he has been the first to ask regular analyses of urine; he also has warned against giving a diet, only because it has a certain amount of calories. He also has proved the importance of physical exercise in diabetes. The rest of the book is devoted to other methods of treatment; they are clearly and shortly described. A number of tables giving recipes for the preparation of various vegetables in the different seasons and of many other things important to medical men treating diabetes. The book can be warmly recommended to those wanting a practical book with a minimum of theory on diabetes.—J. K.

Ueber den Jetzigen Stand der Diabetestherapie (modern views on the treatment of diabetes), by Prof. Carl. van Noorden, Münich & Wiesbaden, 1921. Verlag von J. T. Bergmann, 42 p.

In this brochure the well known investigator describes the different treatments that recently have been recommended in diabetes. He himself recommends a combination of different systems.

I. Days with ordinary diabetes diet, with a protein content of 100-120 gram.

II. Days without meat and cheese with a maximum of 50 grams proteins. Potatoes and fruit must be given in amounts corresponding to 100 gram of bread.

III. Twice a fortnight a carbohydrate day is given. Bananas, apples, and rice, cooked with apples, are of more use than rice or oatmeal.

IV. Each carbohydrate day is followed by a fasting day or a day on which only vegetables are given.

Carbohydrate treatment is indicated in acidosis. Though the administration of alkali is not so dangerous as Joslin believes, van Noorden recommends the use of as little alkali as possible.

—J. K.

DIE UNTERBINDUNG AM HODEN UND DIE PUBERTATSDRUSENLEHRE (THE LIGATION OF THE VAS DEFERENS AND THE THEORY OF A PUBERTY GLAND), by Dr. Hans Tiedje, Jena, 1921. Verlag, von Gustav Fischer, 26 p.

In this small brochure Tiedje describes his experiments on "rejuvenation" in guinea pigs. When one vas deferens is ligated and the other testicle removed in a young animal the remaining testicle develops normally. In older animals the testicle first atrophies, but later shows complete regeneration. In both young and old animals a spermatocele is generally formed. The same results are seen when both vasa deferentia are ligated. When one vas deferens is ligated and the other testicle is not removed the first testis atrophies, while the second shows a compensatory hypertrophy. The author holds that the interstitial cells are of great importance as organs regulating the nutrition of the testicle. He cannot, however, confirm Steinach's theory, by which the interstitial cells are considered to constitute a special gland having a definite endocrine function.—J. K.

BEITRAG ZUR ATROPHIE DES MENSCHLICHEN HODENS (STUDIES ON THE ATROPHY OF THE HUMAN TESTICLE), by Dr. K. Goette, Jena, 1921. Verlag von Gustav Fischer, 26 p.

It is well known that different influences may cause an atrophy of the testicles. Poisons (alcohol), physical influences (x-rays), acute and chronic disease, all may have the same effect. Even when examined histologically the atrophic testicle shows the same picture, whether it is caused by x-rays, by alcohol or by some disease. The atrophy is a primary lesion of the seminal epithelium. The intensity of the atrophy depends on the time, during which the noxious influence lasted and on the general condition of the body. The formation of sperm is much less disturbed in acute disease than in chronic. Whether psychical and physical exertion have an influence on spermatogenesis is not known. This small brochure may be recommended to those making a special study of the gonads and their function.—J. K.

UEBER DIE RUSSISCH-RUMANISCHE KASTRATENSEKTE DER SKOPZEN (CONCERNING THE RUSSIAN-ROUMANIAN CASTRATED SECT OF SKOPTZIES), by Dr. Walter Koch, Jena, 1921. Verlag von Gustav Fischer, 38 p.

The Skoptzies are a religious sect living in Russia and Roumania. Their religion prescribes that male individuals be castrated. They distinguish between the "great operation" when penis and testicles are removed and the "little one" when only the testicles are cut away. Though several authors, notably Pelikan, Tandler and Grosz, and Pittard, have devoted much

labor to the study of this sect, much remains unknown. Koch was able to study certain individuals of the sect during the German occupation of Roumania and he presents his results in this little book, which is enhanced by excellent photographs.

In all cases examined the author found a pale skin, abundant hair of the head, scanty beard, few hairs on the body and in the axillae, female type of pubes, a wrinkled face, small lymphatic apparatus in the throat, small thyroid and long extremities. Koch distinguishes four types of Skoptzies: (7) ordinary type with long extremities; (2) type with giantism; (3) type with acromegaly; (4) type with hypophyseal adiposity. The type seems to depend upon the age at which the operation is carried out. The first type shows a normal sella turcica; in the second the sella seems to be enlarged. In the third class the sella is much larger than normally. Other abnormalities also are apparent in the skull.

The author has carried out exact measurements of the different indices of the body. The book must be considered of

ABDOMINAL PAIN. Prof. Dr. Norbert Ortner, Vienna. Tr. by William A. Brams and Alfred P. Luger. New York, 1922. Rebman Co. 362 p. 8°.

The book is of interest to endocrinologists in that it includes brief discussions of pain associated with some of the endocrinopathies.—R. G. H.

KÖRPERBAU UND CHARAKTER. UNTERSUCHUNGEN ZUM KONSTITUTIONSPROBLEM UND ZUR LEHRE VON DEN TEMPERAMENTEN. Dr. Ernst Kretschmer. 1921. Julius Springer. Berlin. 192 p. 31 pl.

This monograph discusses in an interesting manner the apparent correlation between the various types of body form and the mental and psychic attributes. The point of view is that of the psychiatrist and the examples cited are taken from psychiatric practice. The evident abnormalities in function of the endocrine glands associated with the specific types discussed are brought out. Temperament is considered as a matter of humoral or blood chemistry, the body representative of which is the brain-endocrine gland system. The publication can be recommended to both the endocrinologist and the psychiatrist.—F. S. H.

THE AUTONOMIC NERVOUS SYSTEM. J. N. Langley. Cambridge, 1921. W. Heffer & Sons, Ltd. 80 p.

Reviewed by Prof. Sherrington in Physiol. Abst., 1922, **6**, 650.

HORMONES AND HEREDITY. A discussion of the evolution of adaptations and the evolution of species. J. T. Cunningham. London, 1921. Constable & Co., Ltd. 246 p.

After an introduction giving a historical survey of theories or suggestions of chemical influence in heredity, there follow chapters on classification and adaption, mendelism and the heredity of sex, influence of hormones on development of somatic sex characters, origin of somatic sex characters in evolution, mammalian sexual characters, evidence opposed to the hormone theory, origin of non-sexual characters, the phenomena of mutation, metamorphosis and recapitulation.

Cunningham believes that there are two distinct kinds of characters in all organisms, namely, those of somatogenic origin and those of gametogenic origin. Somatic modifications by means of hormones affect the determinants in the gametes. His theory supposes that every part of the body gives off special substances which have a special effect on the corresponding parts of the chromosomes. He even suggests that bones of different parts of the body give off different hormones. In discussing the development of the antlers of the stag it is supposed that an exostosis formed on the frontal bone as a result of repeated mechanical stimulation, due to the butting of stags, gives off an increased quantity of intermediate waste products of the same kind as the tissues from which it arose gave off before. These products act as a hormone on the gametocytes, stimulating the factors which in the next generation would control the development of the frontal bone and adjacent tissues. There are two hormone actions, the centripetal from the hypertrophic tissue to the corresponding factor in the gametocytes and the centrifugal from the testes to the tissue of the antler or other organ concerned.

Cunningham uses the term hormone in Starling's original sense, and includes all kinds of products of metabolism in the category. He argues that if the intestinal glands can produce an internal secretion, so also can other tissues. It is true that Starling originally referred to CO_2 as a hormone. We are not in a position to deny that all products of metabolism have an influence on the economy. On the other hand the majority of investigators at the present time do not admit that we have any evidence that such is the case.

The author believes in the inheritance of acquired characters. "There exists very good evidence that modifications due to external stimulus do not perish with the individual, but are in some degree handed on to succeeding generations."

The book is well written and beautifully illustrated.—S. V.

THE VITAMINES. H. C. Sherman and S. L. Smith. N. Y., 1922. The Chemical Catalog Co. 273 p. 8°, 3 pl.

While vitamines are, so far as known, not internal secretions, endocrinologists, no doubt, in view of their interest in metabol-

ism, will be largely interested in this book. It takes up the history of vitamines and then treats successively of vitamines, A, B and C. A final chapter is devoted to vitamines in the problem of food supply. The evidence is succinctly but readably presented. The book closes with a valuable twenty-seven page bibliography.
—R. G. H.

Los Mechanismos de Correlación Fisiológica. Augusto Pi Suñer. Barcelona, 1921. P. Salvat. 299 p. 8°.

The book comprises a series of eighteen lectures delivered before the Faculty of Medical Sciences of Buenos Aires in 1919. As suggested by the title, the author takes up the various mechanisms by which physiological unity is attained. Cellular as well as nervous and hormone correlations are considered. Endocrinologists who are able to read Spanish will find the book an interesting exposition of the fundamental philosophy of their problems.—R. G. H.

The Morphologic Aspect of Intelligence. Sante Naccarati. Columbia University Contributions to Philosophy and Psychology, Vol. 27, No. 2. N. Y., 1921. 44 p. 8°.

The book comprises a terse presentation of certain anthropologic and psychologic data from which the author draws various deductions of interest to the endocrinologist. Among the three morphologic types differentiated by Viola, viz., the microsplanchnic, the normosplanchnic and the macrosplanchnic, the microsplanchnic gives the more intelligent units. Normosplanchnics represent all degrees of intelligence. Macrosplanchnics, while representing a less intelligent group, individually may be as intelligent as any other type. The microsplanchnic type is mentally hyperevolute. This fact constitutes another proof in support of Viola's thesis that the macrosplanchnic type and not the microsplanchnic is an infantile type and therefore retarded in development. The microsplanchnic type corresponds to the hyperthyroid type, namely, that marked by a constitutionally hyperactive thyroid, an "Orthoplastic hyperthyroidism" (Pende), or a "Hyperthyroid temperament" (Levi and Rothschild). The morphologic type is the outcome of hereditary and accidental factors. Hormonic actions, which influence the physical and mental growth, the metabolism, and the nervous reactions, are in part responsible for the individual differences in the same family and in the same ethnic group. During the prenatal life and during infancy and the adolescent period, environment, diseases, traumata (physical and moral), improper diet, etc., may affect the function of one or more endocrine glands, and thus produce morphologic deviations which are usually accompanied by

mental deficiencies or gains on account of interrelations existing between the morphoregulator and the neuroregulator hormones.
—R. G. H.

STUDIES IN DEFICIENCY DISEASE. Robert McCarrison, London, 1921. Henry Frowde and Hodder and Stoughton. 270 p.

For review see Am. J. M. Sc., 1922, **163**, 440-441. The monograph apparently is a compilation of the author's valuable studies previously published in the periodical literature. Many of the data are of interest to endocrinologists. They have appeared or will appear in this Journal in abstracts of the original articles.—R. G. H.

EPREUVE DE GOESCH. Sigismond Bloch. Paris, 1921. Vigot Frères. 77 p. 8°.

Bloch reports in some detail the results of the Goetsch epinephrin test in a variety of clinical conditions in forty-eight subjects. Definitely positive results were obtained in two cases of goitre—toxic and exophthalmic—one case of pluriglandular insufficiency, six of infection, two of diabetes and one of pregnancy. Partially positive reactions were seen in three cases of Graves' disease, one of infantile myxedema, under thyroid treatment, three of infection, two of diabetes and one of chronic alcoholism. Negative tests were obtained in twenty-two cases. These included two of "Basedowified" goitre, one of five years' standing and the other in a pregnant woman; one doubtful case of Graves' disease; one of myxedema; six acute infections; five chronic infections; one chronic alcoholism; one dysenteriform colitis; one mitral regurgitation; one myopathy; three infantilism. The author was impressed with the fact that cases taken at random in the great majority of instances give negative tests and that the positive tests are mostly obtained in cases in which thyroid involvement is common or essential. On the whole, the test is regarded as valuable.—R. G. H.

THE JOURNAL OF BIOCHEMISTRY. Motofujicho, Hongo, Tokyo, Japan. Editor-in-chief, Prof. Samuro Kakiuchi. Vol. 1, No. 1, January, 1922.

A new journal devoted to publication of work by Japanese investigators. Articles are published in English, French and German, predominantly, but any language written in Roman characters is acceptable.

THE JOURNAL OF METABOLIC RESEARCH. Vol. 1, No. 1. Jan., 1922.

A new journal devoted to the publication of original investigations in the field of metabolism. Edited by Frederick M. Allen. Published monthly by "The Physiatric Institute," Morristown, N. J.—R. G. H.

Abstract Department

Clinical considerations of some cases of ACROMEGALY (Consideraciones clinicas sobre algunos casos de acromegalia). Martinez (G. N.) & Moyano (J. J.), Rev. del Circulo méd. de Cordoba, 1921, **9**,—(Nos. 5, 6, 7, 8).

This article gives an account of three cases of acromegaly observed at different periods of life; one in youth (24 years), the other two in maturity (51 and 61 years, respectively). All three showed typical manifestations of diabetes insipidus and latent or evident bitemporal hemianopsia. In two cases radiographs disclosed enlargement of the sella turcica. There was perfect and even augmented carbohydrate tolerance.—B. A. H.

(ADRENALS) Hyperchlorhydria in childhood. Berman (L.), New York M. J., 1921 **114**, 226-228.

The occurrence of hyperchlorhydria is commonly produced in a certain class or type of children by irritating foods. Such children are generally of dark complexion, and have a tendency to low blood pressure, low blood sugar and relatively abnormal fatigability. This predisposition perhaps depends upon a certain relation to the **adrenal-sympathetic-thyroid** mechanism of the organism which controls the conductivity of nerves inhibiting or stimulating the gastric cells. Such cases do well under a hygienic regime with removal of the gastric irritants from the diet, antacids and adrenal nucleoprotein.—H. W.

(ADRENIN) Respiratory metabolism in toxic glycemias (Ueber den Respiratorischen Stoffwechsel bei toxischen Glykämien). Bornstein (A.) & Müller (E.), Biochem. Ztschr. (Berl.), 1921, **126**, 64-76.

Studies on dogs and man with pilocarpin and adrenalin, the former a stimulant of the parasympathetic, the latter of the sympathetic nervous system. Pilocarpin administration is immediately followed by an increase in the respiratory quotient which must be attributed to an increased sugar oxidation. Adrenalin did not produce the rise in respiratory quotient.—F. S. H.

The vascular-leucocyte formula after ADRENALIN injections (La formule vasculo-leucocytaire après injection d' adrénaline). Danul (N.) & Popper (M.), Ann. de méd. (Paris), 1921, **10**, 395-399.

Studies on 14 normal (?) persons. The intravenous injection of 0.0005 to 0.001 mg. adrenalin produces a quick hypertension lasting 3-4 minutes. This is accompanied by a hyperleucocytosis in the majority of cases. The leucocyte formula is variable. These phenomena are believed to be purely mechanical results of arterial tension and not of specific excitation of the hematopoietic centers.
—F. S. H.

Cold abscess of the ADRENALS (Abcès froid des capsules surrènales). Deglos (E.), Lyon méd., 1921, **130**, 523-528.

According to Deglos, who records an illustrative case in a woman, aged 28, rapid and complete cessation of both suprarenals with transformation of one of them into a large cold abscess is rare, especially when most of the symptoms of Addison's disease are absent. Deglos' case took the form of an attenuated septicemia, with a temperature which suggested typhoid or paratyphoid fever. Death took place suddenly. In addition to the suprarenal lesions the autopsy showed marked hypoplasia of the **ovaries** and slight **thyroid** hypoplasia. Deglos suggests that in an infective process in which several blood cultures do not explain the cause of the condition, the possibility of a cold suprarenal abscess should be considered, when very pronounced hypotension is associated with extreme prostration without the presence of other signs of chronic epinephritis.—Med. Sci., **5**, 306.

(ADRENIN, HYPOPHYSIS) The pharmacology of chelidonin, the benzylisoquinoline alkaloid of chelidonium. Hanzlik (P. J.), J. Pharmacol. & Exper. Ther. (Balt.), 1921, **18**, 63-102.

Chelidonin antagonizes the augmentor effects of pituitary extract on the intestine and uterus and that of epinephrin on the pregnant uterus.—F. A. H.

The influence of ADRENALIN on the white blood cell picture (Suprareniwirkung auf das weisse Blutbild). Hess (O.), München. med. Wchnschr., 1921, **68**, 1668.

After injection of adrenalin the number of leucocytes is increased, lymphocytes often at first predominating, giving the so-called diphasic blood picture. This, however, is not at all regularly observed. In two cases of pernicious anaemia the behavior of the lymphocytes was identically the same two days before and after removal of the spleen.—J. K.

Antagonistic action between atropine and ADRENALIN upon the vascular system of frogs (Über einen Antagonismus zwischen Atropin und Adrenalin am Gefässapparat des Frosches). Hildebrandt (F.), Arch. f. exper. Path. u. Pharmakol. (Leipz.), 1920, **86**, 225-237; Ber. ü. d. ges. Physiol. (Berl.), 1921, **3**, 340.

On the Läwen-Trendelenberg frog preparation atropine has no influence. If, however, one maintains the blood vessels in a state of constriction by long perfusion of adrenalin in concentration of 1:500,000 to 1:2,000,000 atropine may result in relaxation, proportional to the amount employed. In the splanchnic area, atropine causes constriction of the vessels; but just as in the skin-muscle area it releases the constriction caused by adrenalin although the action is weaker. On the other hand, by prolonged infusion with atropine in Ringer's solution (1:10,000 to 1:2,000) both irritability to sympathetic stimulation and to adrenalin is either lost or much diminished. Since $BaCl_2$ maintains its constrictor effect throughout atropine perfusion, the author believes that the inhibitory action of atropine is manifested either in the adrenalin-sensitive substance or between this and the part of the apparatus sensitive to $BaCl_2$.

—R. G. H.

Technique of the extirpation of the medullary part of the ADRENALS (Technique de l'extirpation de la partie médullaire des surrénales). Houssay (B. A.) & Lewis (J. T.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1209-1210.

In this article a simple method of removing the adrenal medulla and maintaining the cortex in good condition is illustrated. The directions are fairly full.—T. C. B.

Comparative importance of the medullary and cortical parts of the ADRENALS (Importances comparatives des parties médullaire et corticale des surrénales). Houssay (B. A.) & Lewis (J. T.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1210-1212.

The suprarenal medulla on the left side was extirpated in sixteen dogs, then after ten to fifteen days the right suprarenal was totally extirpated. Three dogs died within forty-eight hours of the operation. One escaped in good health and two were kept for three months in perfect health. The other ten were sacrificed for other purposes. Histological examination of the five dogs that died early or were killed showed total absence of medullary substance in four, and a minute trace in one. The authors think the three dogs that died in forty-eight hours had gross lesions of the cortex, which was the cause of death.—T. C. B.

(ADRENALIN) Experiments on vasoconstrictor substances in the blood in high blood pressure (Untersuchungen über gefaszverengernde Stoffe im Blute bei Hypertonien). Hülse (W.), Zentralbl. f. innere Med. (Leipz.), 1922, **43**, 1-7.

Although many believe hypertonia due to hyperadrenalinemia, Hülse was never able to confirm this. Even in cases with an enormously high blood pressure no hyperadrenalinemia nor increases in other vasoconstrictor substances were found. Some authors reg-

ularly find hyperglycemia in hypertonia, but if this were true it could not be explained as an adrenalin glycosuria. The author found that the serum of patients with Bright's disease, when injected into a normal animal, increases the sensibility of the blood vessels for adrenalin.—J. K.

(ADRENALIN) Un caso de hipervagotonia. Izquierdo (J. J.), Rev. Mex. de biol. 1921, **1**, 124-133.

The data in somewhat abbreviated form were published in Endocrin. 1921, **5**, 607-609.

The toxicity of the blood of ADRENALECTOMIZED frogs. Kellaway (C. H.), J. Pharmacol. & Exper. Therap. (Balt.), 1921, **18**, 399-405.

The adrenals were destroyed by cautery. Frogs used for testing were perfused through a sinus cannula. Of the serum to be tested, 0.2 cc. was added to 2 cc. of perfusion fluid. The most striking feature of the symptom complex next to paralysis of the lower limb was progressive slowing of the respiration. Neither the serum of frogs dying from decapsulation nor the serum of decapsulated frogs killed when evidently moribund "gave unequivocally positive results."—F. A. H.

The theory of ADRENALIN formation (Zur Theorie der Adrenalin-Bildung. Erwiderung auf die Bemerkungen von K. Rosenmund und H. Dornsaft). Knoop (F.), Ber. d. deutsch. chem. Gesellsch. (Berl.), 1920, **53**, 716-718; Abst., Ber. ü. d. ges. Physiol. (Berl.), 1921, **4**, 19.

Rosenmund and Dornsaft's theory of adrenalin formation stands without biological analogy. Although it can be shown that adrenalin may be produced from tyrosin (or dioxyphenylalanin) the necessary assumption of the formation of an alcoholic hydroxyl group still remains to be overcome.—R. G. H.

(ADRENALS) Pathology of cholesterol metabolism. Krontovsky (A.), Pub. Kiev. Univ., 1918.

The quantity of cholesterol in horse-serum was increased by long-continued feeding with dried brain; the amount was increased by 66 per cent after 28 days of such a diet; the internal organs did not show any modification. In another horse, which, besides this diet, was immunized by the diphtheria toxin, hypertrophy of the cortex of the suprarenals was observed as well as increase of quantity of anisotropic lipoids. Immunisation alone produced the same result.—Physiol. Abst., **5**, 53.

The ADRENALS and morphin intoxication (Les surrénales et l'intoxication par la morphine). Lewis (J. T.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1214-1215.

It has been shown that decapsulated rats and frogs are very sensitive to morphin. The present paper deals with the results of experiments on dogs. The results are not so clear as in frogs and rats, but appear to support the idea that decapsulated dogs are more sensitive to morphin than the controls. Morphin, even in anesthetic doses, shortens the survival of decapsulated dogs.

—T. C. B.

A clinical note on latent malaria and on the influence of ADRENALIN (Nota clinica sulla malaria latente e sull'azione della adrenalina). Levi (E.), Gazz. d. osp. (Milano), 1921, **42**, 1185-1188.

When 1-2 mgm. of adrenalin is injected into a patient with latent malaria there are three possible results: (1) a typical attack of malaria with plasmodia in the blood; (2) a light attack with plasmodia; (3) a rise in temperature. If no reaction occurs the malaria is cured. A rise of temperature after the injection of adrenalin may also be seen in patients recovering from typhoid fever, erysipelas, and, sometimes, tuberculosis. The vaso-constrictor action and the increased blood pressure may stimulate the heat center.—J. K.

(ADRENIN) Response to drugs of excised bronchi from normal and diseased animals. Macht (D. I.) & Ting (G. C.), J. Pharmacol. & Exper. Therap. (Balt.), 1921, **18**, 111-119.

Bronchial rings or bronchial strips of the pig in Locke's solution were used. It was found that in pathological conditions there is an impairment of the normal physiological properties so that epinephrin may have little or no effect on bronchial muscle.

—F. A. H.

(ADRENIN) A study of antispasmodic drugs on the bronchus. Macht (D. I.) & Ting (G. C.), J. Pharmacol. & Exper. Therap. (Balt.), 1921, **18**, 373-398.

Excised bronchial preparations were used. The most powerful dilators were: First, papaverin and various benzyl compounds, which act on muscle cells; second, atropin, which paralyzes parasympathetic myoneural junctions; and third, **epinephrin**, which stimulates the sympathetic.—F. A. H.

Is ADRENALIN a hormone (E' L'adrenalina un ormone)? Marfori (P.), Gazz. d. osp. (Milano), 1921, **42**, 1096; Arch internat. de pharmacod. (Gand & Par.), 1921, **26**, 137-149; Abst. Ber. ü. d. ges. Physiol, **11**, 109.

Gley has cited evidence that the blood in the vena suprarenalis does not contain adrenalin. He stimulated the splanchnic nerve in a dog and at the same time took some blood from the suprarenal

vein. This was injected into another dog; no change in blood pressure resulted. Marfori believes that the quantity of blood used by Gley was too small. He repeated Gley's experiments, only instead of stimulating the sympathetic he injected a small dose of adrenalin intravenously. Then 30 cc. of the arterial blood of the animal was injected into a second. No rise of blood pressure occurred. This proves that small doses may be present without being detected by Gley's method.—J. K.

A new case of ADRENAL virilism (Un nouveau cas de virilisme cortico-surrénal). Mauclaire (P.), Bull. Acad. de méd. (Par.), 1920, 3.s., **84**, 57-58.

According to Mauclaire, who records an illustrative case, Apert in 1910 collected 30 cases of suprarenal hypertrophy or tumors of the suprarenal cortex which had given rise to a masculine appearance in women. Blanchard, in 1916, in a study of the pathogeny of suprarenal virilism, came to the conclusion that this condition was due to changes in the interstitial gland of the **ovary**, an opinion shared by Pierre Marie. Symptoms of virilism may also appear at the **menopause**, but they are not so marked as they are in suprarenal virilism. Mauclaire's case was a woman aged 38, who, six years previously, had developed an abdominal tumor, and at the same time had cessation of her menses. Her face, neck, and chest became covered with numerous long hairs, the face became elongated, the breasts atrophied, and the body lost its rounded form. Laparotomy revealed the presence of a tumor of the right suprarenal. The patient was subsequently treated with ovarian extract and her catamenia reappeared.—Med. Sci., **3**, 218.

(ADRENIN, PITUITRIN) The activity of the isolated uterus. Ogata (S.), J. Pharmacol. & Exper. Therap. (Balt.), 1921, **18**, 185-200.

In the rabbit adrenalin caused an increase in tonus and in rate in the longitudinal muscle of the uterus, while the contraction of the circular muscle was increased in rate. After atropin, adrenalin always produced a temporary inhibition both of circular and longitudinal muscle. After ergotoxin adrenalin produced a like effect. Pituitary extract often produced inhibition although usually an increase in tonus occurred in both the virgin and pregnant uterus. In the rat, adrenalin caused relaxation while pituitary extract caused contraction of the uterus.—F. A. H.

Latent ADRENAL insufficiency rapidly developing after trauma. Death after surgical intervention. Total destruction of the two capsules by tuberculous caseation (Insuffisance surrénale latente. Evolution rapide après un traumatisme. Mort subite après intervention chirurgicale. Destruction totale des deux capsules par

caséification tuberculose). Oudard, Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 184-188.

The title tells the story.—F. S. H.

Is ADRENALIN conducted along the nerves (L'adrenaline est-elle conduite le long des nerfs)? Rebello (S.) & Pereira (M. de M. B.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1163-1165.

It has been maintained by Lichtwitz and denied by Meltzer that adrenalin can be conducted along nerve trunks. The authors have made eighteen experiments, employing the methods of Lichtwitz, and obtained positive results in fourteen cases. The latent period between injection and response was about 32 minutes. They conclude that the phenomena observed by Lichtwitz (cutaneous hypersecretion and dilation of the pupil) are undeniable.—T. C. B.

The mechanism of the action of ADRENALIN at a distance (Sur le mécanisme de l'action a distance de l'adrenalin). Rebello (S.) & Pereira (M. de M. B.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1166-1168.

As the injection of adrenalin into a frog's hind leg attached to the body only by the sciatic nerve, gives rise to a sympathicotonic syndrome (exophthalmos, mydriasis and cutaneous hypersecretion), it is necessary to determine the mechanism of this action. The operation itself, the injection of air, the production of pain, does not cause the symptoms. Injection of adrenalin into the dorsal lymph sac, or into a normal limb always produces the symptoms in from five to ten seconds. With the sciatic nerve as the only bridge of communication between the amputated limb and the rest of the body, it was found that the injection of simple Ringer's solution gave results comparable to those obtained with adrenalin in 50 per cent of the cases. Injection of atropine causes mydriasis and augmentation of the cutaneous secretions. Eserine causes hypersecretion, and pupillary dilation. In animals that react in this way, a second injection, if that injection is adrenalin, is followed by a stronger reaction than the first. The injection of cocain, or placing a bit of cotton soaked in cocain on the sciatic, prevents the development of symptoms. The conclusion is that adrenalin is not conducted along the nerves, but the excitation is, and that adrenalin may have a specific exciting action. The long latent period is difficult to explain. It may be due to slow imbibition or slow penetration of adrenalin.—T. C. B.

Graves' disease and the ADRENAL glands (La maladie de Basedow et les capsules surrénales). Swiecicki (H.), Presse méd. (Par.), 1921, **29**, 664-665.

Swiecicki, of Posen, is inclined to regard Graves' disease as due to hyperactivity of the suprarenals, the vasomotor and secretory

symptoms, including tachycardia, tremor, and exophthalmos, being caused by an increase of secreted adrenalin. He therefore recommends that treatment should aim at diminishing the production of adrenalin by administration of oil of sesame and hypotensive measures, including mild hydrotherapy, rest, and residence in a mountainous climate.—Med. Sci., **5**, 301.

The functional connection between the glandular portion of the OVARY and the ADRENAL cortex. Serdioukov (M.), Vratchebnoïé Délo (Kharkov), 1921, **2**, (No. 16-21): abst. Presse méd., 1922, **30**, 130.

Serdiokov of the Laboratory of Experimental Pathology at the University at Saratov has carried out a series of experiments on pregnant and non-pregnant cats with a view to determining certain endocrine interrelationships. As a result of the variations in the cytological picture of interstitial cells of the ovary, the **corpus luteum** and the suprarenal cortex, he concludes that these glands stand in vicarious relationship with each other. This conclusion is fortified by the fact that the secretion of each tissue is of lipoid nature.—R. G. H.

(ADRENALS) The relation of melanin formation in the skin to Addison's disease (Des mélanodermies du type Addisonien). Sézary (A.), Presse méd. (Par.), 1921, **29**, 281-283.

Sézary remarks that the sympathetic system has long been regarded as responsible for the pigmentation found in Addison's disease, but he can find no adequate evidence for this hypothesis. On the other hand, he marshals many facts which tend to show that this pigmentation is due to an increase of the normal melanin-forming function of the skin and that this increased function is brought about by various endocrine disorders. He does not suggest that any one of the **endocrine glands** is alone to blame.—Med. Sci., **5**, 306.

Total ADRENAL insufficiency. Asthenia and intoxication (Insuficiencia adrenalinica total. Astenia e intoxicación). Soler (F. L.), Semana méd. (Buenos Aires), 1921, **28**, 361.

Dogs under chloral-morphine anesthesia died within 13 hours after bilateral extirpation of the two suprarenal glands. Their cerebral motor zone was not irritable and they gave a practical demonstration of the final conclusion of Cheyne-Stokes syndrome. Soler concludes that capsular insufficiency produces death by facilitating morphine poisoning.—B. A. H.

(ADRENIN) The sensitiveness to poisons in avitaminous animals. Van Leeuwen (W. S.) & Verzar (F.), J. Pharmacol. & Exper. Therap. (Balt.), 1921, **18**, 293-311.

Among other things the blood pressure reaction to adrenalin of normal and avitaminous fowls and cats was studied. The reaction did not differ materially in the two cases. It was concluded that the decreased activity of smooth musculature in avitaminosis is probably caused by a lack in the body of these animals of the normal chemical agents.—F. A. H.

Paradoxical behavior of sugar metabolism on the simultaneous administration of pilocarpin and ADRENALIN ("dissimilatory conversion") [Ueber ein paradoxes Verhalten des Zuckestoffwechsels bei gleichzeitiger Einwirkung von Pilocarpin und Adrenalin ("Dissimilatorische Umkehr")]. Vogel (R.) & Bornstein (A.), Biochem. Ztschr. (Berl.), 1921, **126,** 56-63.

Although both adrenalin and pilocarpin, when given separately, induce hyperglycemia, when they are administered simultaneously there results at first slight hypoglycemia, which is later followed by a rise in blood sugar. This is interpreted as indicating that the pilocarpin hyperglycemia mechanism differs from that of adrenalin hyperglycemia.—F. S. H.

BLOOD SUGAR metabolism (Blutzuckerstoffwechsel). Meyer (E.), Berl. klin. Wchnschr., 1921, **58,** 1542-1543.

When normal individuals, patients with epilepsy, dementia paralytica, icterus, or encephalitis take 20 grams of glucose on an empty stomach they show a rise of the blood sugar with its maximum in the second half hour after the injection. When, later, 100 grams of glucose is given the blood sugar rises only in icterus and in nitrobenzol intoxication. In **diabetes** the rise of the blood sugar after 20 grams of glucose is much more intense. The regulation of the blood sugar depends upon the **liver,** the **pancreas,** the bowels, the central nervous system and the **endocrine organs.**—J. K.

The BLOOD SUGAR in surgical diseases (Das Verhalten des Blutzuckers bei chirurgischen Erkrankungen). Seitz (E.), Mitt. a d. Grenzgeb. d. Med. u. Chir. (Jena), 1922, **34,** 514-526.

Some time ago the author published in Arch. f. klin. Chir., Vol. 112, observations to the effect that in patients who have a high alimentary hyperglycemia without **diabetes,** infections with staphylococci are extremely frequent. He now has examined other diseases. He found that in tuberculosis, also, there is very often a marked alimentary hyperglycemia. This is not due to cachexia, since it is not found in cancer. The blood sugar was studied in cases of **Graves' disease** also, and the alimentary hyperglycemia was found to be high. This is probably due to the increased irritability of the **sympathetic system.** It was found that 14 days after an operation for Graves' disease the sugar metabolism and the tonus of the involuntary nervous system had become normal. It

is remarkable that in some cases of diffuse **colloid goiter** after strumectomy alimentary hyperglycemia and the sympathetic tonus were increased. Seitz believes that Graves' is a primary thyroid disease. If this were not true, it would be difficult to explain why sugar metabolism becomes normal almost immediately after strumectomy. The rapid restoration of carbohydrate equilibrium shows also the excellent results of surgical treatment in Graves' disease.
—J. K.

CHOLIN as a peristaltic hormone (Cholin als Hormone der Darmbewegung). Magnus (R.), Naturwissenschaften, (Berl.), 1920, **8,** 383-388.

After a general account of intestinal movement, the author goes on to allude to the work of le Heux, who regards choline on experimental evidence as the main chemical stimulus of Auerbach's plexus, and fully endorses this view. The origin of choline is the lecithin of protoplasmic cells; its activity is controlled by some antagonistic substance with the same action as atropine, and may be intensified by the formation of certain esters as in acetylisation (Dale, Reid Hunt). If this occurs in the intestine the presence of synthetic enzymes capable of forming choline esters is postulated. It is possible that choline may play a similar rôle in other organs. —Physiol. Abst., **5,** 415.

The influence of Karlsbad water and salt on DIABETES, and a new theory on this disease (Die Wirkung des Karlsbader Wassers und Salzes auf Zuckerkranke, beurteilt nach einer neuen Auffassung über den Diabetes). Arnoldi (W.) & Roubitschek (R.), Deutsche med. Wchnschr. (Berl.), 1922, **48,** 250-251.

The authors introduce a new theory on diabetes. They believe that it is caused by a disturbed transport of the sugar through the body. The cells are less permeable for glucose on account of a change in the protoplasm. The protoplasm is probably changed by an abnormal proportion between K, Na, Ca, etc., ions. The excellent results procured by the use of Karlsbad water may be due to a restoration of the normal proportion of metallic ions. Ordinary water, when ingested by a normal person, has no influence on the **blood sugar;** when Karlsbad water is given the blood sugar sometimes sinks, sometimes is not affected. In the majority of cases of diabetes the blood sugar sinks, sometimes even very markedly, after the ingestion of Karlsbad water.—J. K.

DIABETIC retinitis (Rétinite diabétique). Chauffard (A.), J. des Praticiens (Par.), 1922, **36,**—(No. 3); Abst. Presse méd. (Par.), 1922, **30,** 155.

The case is described of a woman of 78 who had had visual troubles for two years. There was also latent or slight glycosuria

and glycemia of 3 gm., but with good general health and no other diabetic signs except that the ophthalmoscope showed retinitis similar to that of albuminuria or nephritis. There was, however, no albuminuria nor increased blood nitrogen. Such findings are characteristic also of retinitis of pregnancy. The author explains the common retinoscopic picture in each of these conditions as due to a concomitant cholestrinemia. He assumes that the excessive amount of circulating cholesterin leads to its deposit in the inflammatory exudates.—R. G. H.

Curve of sugar excretion in severe DIABETES. Felsher (H.), J. Biol. Chem. (Balt.), 1922, **50**, 121-129.

"The work reported in this paper represents a study of the total quantities of sugar excreted in a number of diabetic patients during periods in which they were being held in the non-diabetic status by dietary restriction, and during the periods in which the diets were gradually increased until clearly abnormal quantities of sugar appeared in the urine." "Study of the curves obtained lead to the conclusion that individuals with severe diabetes, when brought into the non-diabetic status, by fasting or other more suitable adjustments of the diet, may then excrete small quantities of sugar not greater than those excreted by normal individuals under parallel conditions. The quantities in the series averaged 10 and 15 mg. per kilo per day. As the diet is gradually increased step-wise at 1 to 4-day intervals there is at first little or no permanent increase of the sugar excretion." When the total glucose equivalent of the diet has risen above a certain limit (which varies with the individual), however, further additions to the diet lead to sudden and rapid accelerations of sugar excretion out of proportion to the preceding output. This observation is in harmony with the well known conception of a clearly definable "tolerance limit" for glucose in diabetes.—F. S. H.

Modern theories and treatment of DIABETES (Die moderne Entwicklung der Theorie und der Therapie des Diabetes mellitus). Frank (E.), Wien. klin. Wchnschr., 1921, **35**, 70-71.

This article is a good, brief, up-to-date general review, without new data.—J. K.

Pancreatic DIABETES in dogs deprived of the ADRENAL medulla (Diabète pancréatique chez les chiens privés de la partie médullaire des surrénales). Houssay (B. A.) & Lewis (J. T.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1212-1213.

Five dogs were operated upon. The medulla of the left suprarenal was extirpated, then the right suprarenal gland. About one month later the entire pancreas was removed. Two dogs survived, one eight days and one three days. Both had hyperglycemia and

glycosuria. Histologically there was complete absence of medullary substance in one case, and a minute fragment in the other (eight days of diabetes with the strongest glycosuria). The other three presented no variation in glycemia. One did not eat and died of peritonitis four days after pancreatectomy. The other two died six and twenty-four hours after a difficult pancreatectomy.

—T. C. B.

Secondary DIABETES in pigmentary cirrhosis (Le diabète secondaire dans la cirrhose pigmentaire). Lereboullet (P.) & Mouzon (J.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **45**, 1681-1689.

The important point in this case report is the tardy appearance of diabetes some four years after the onset of pigmentation and hepatomegaly.—F. S. H.

Organotherapy in DIABETES (Ueber Organotherapie bei Diabetes mellitus). Loening (K.) & Vahlen (E.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 217-219.

Vahlen has prepared a substance from the pancreas of a cow, which he calls metabolin. There is a substance in yeast differing only slightly from metabolin. Administration of this substance to diabetics has one of three effects: (1) Absolutely no result; (2) incomplete result, the sugar in the urine being diminished; (3) complete result, the sugar disappearing. Some case reports are given. The authors fail to tell the preparation of the substances used and do not give the quantity of blood sugar, which is much more significant than urine sugar.—J. K.

A study of the Wassermann reaction in 140 cases of DIABETES mellitus. Rosenbloom (J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **18**, 236.

In a study of 140 cases of diabetes mellitus, a positive Wassermann reaction was found in sixteen cases. Eight of these presented signs of tertiary syphilis. These eight were treated for the existing syphilis. There was no increase in tolerance for carbohydrate following the treatment. This may be due to the fact that the fibrosis of the pancreas produced by the syphilis is not changed by the treatment.—R. G. H.

Blood pressure studies in 140 cases of DIABETES mellitus. Rosenbloom (J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **18**, 236-237.

Blood pressure estimations were carried out on 140 cases of diabetes for varying lengths of time. Some have been studied for as long as ten years. It appears that the blood pressure in un-

complicated diabetes is normal or slightly under normal. In every case of elevated blood pressure in this series were found complications such as aortitis, arteriosclerosis, nephritis, cardiac hypertrophy and aortic endocarditis. In conditions of acidosis the blood pressure falls. The presence or absence of hyperglycemia had no effect on the blood pressure.—R. G. H.

Treatment of DIABETES (Behandlung des Diabetes). Schreiber (E.), Berl. klin. Wchnschr., 1921, **58**, 1543.

Not too much protein and much fat is the best diet in diabetes. The "Mehlfrüchtekur" of Falta may be recommended. No novel data are offered.—J. K.

Relation between DIABETES and syphilis (Contribution a l'étude des rapports du diabète et de la syphilis. Un casa de diabète sucré apparu quelques jours après un chancre syphilitique). Vallaret (M.) & Blum (P.), Bull. et mém. Soc. méd. d hôp. de Par., 1922, **46**, 90-94.

Report of a patient who developed diabetes a few days after chancre. The patient had not been previously diabetic. Diabetes developed side by side with the syphilis.—F. S. H.

DIABETES INSIPIDUS. Anon., Med. Sci. (Lond.), 1922, **5**, 396-401.

An interesting review of some of the more important recent literature.—R. G. H.

(DIABETES INSIPIDUS) The rhythm of hypophysary polyuria. Bergé (A.) & Schulmann (E.), Med. Press. & Circ. (Lond.), 1921, **i**, 454-456.

Bergé and Schulmann summarize the characteristics of the polyuria in diabetes insipidus as follows: (1) The quantity eliminated is variable, no approximate figure being assignable; (2) The polyuria is more pronounced at night; (3) The quantity of urine excreted is at times greater than that of the fluid ingested (dehydration); (4) There are no notable modifications of the excretion attributable to variations of régime; (5) There is no important disturbance of the chemical composition of the urine; generally speaking there is a slowing of metabolism and a tendency to demineralization; the amount of uric acid is small; there is no glycuronic disturbance; (6) Absolute renal integrity has been verified by (a) elimination of methylene blue, (b) persistence of the faculty of ureal concentration and maintenance of normal quantity; (7) Controlling action of extract of the posterior lobe of the hypophysis on the polyuria.—Med. Sci., **5**, 398.

DIABETES INSIPIDUS complicated by intermittent glycosuria. Evans (G.) & Wallis (R. L. M.), Lancet (Lond.), 1921, **1**, 70-72.

Evans and Wallis record two cases of diabetes insipidus complicated by glycosuria, the intermittent nature of which distinguished them from the cases of diabetes innocens described by Salomon. The writers regard the cases as examples of a pituitary dystrophy comparable to those cases of thyroid dystrophy in which there is no marked change in the size of the gland and no distinct clinical picture of either hypo- or hyper-function.—Med. Sci., **5**, 398.

Gastro-intestinal conditions in DIABETES INSIPIDUS (Uber das Verhalten der magen-und Darmfunktion beim Diabetes insipidus). Gorke (H.) & Deloch (E.), Med. Klin. (Berl.), 1921, **17**, 1140-1142.

Gorke and Deloch, of the Breslau University Medical Clinic, report three cases of diabetes insipidus in which, in addition to polyuria, polydipsia, anhydrosis, and increase in molecular concentration of the blood, the following gastro-intestinal symptoms were found, viz.: Hyperacidity, hypersecretion, increased gastric peristalsis and spastic constipation of the large intestine. The writers regard these disturbances of gastro-intestinal function as connected with the lability of the **vegetative nervous system** present in these cases, and attribute the favorable effect of **pitu-glandol** on the symptoms either to its direct action or to indirect action by the agency of the vegetative nervous system.—Med. Sci., **5**, 399.

Treatment of DIABETES INSIPIDUS with PITUITRIN and pituglandol (Diabète insipide traité par la pituitrine et le pituglandol). Urechia (C. I.) & Alexandrescu-Dersca (C.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 190-195.

Report of one case, female, aged 35 years. The polyuria was alleviated by injections of pituitary preparations. The diminution was in general proportional to the size of the dose.—F. S. H.

Diseases of the DUCTLESS GLANDS. Rolleston (J. D.) & "G. W.," Med. Sci., 1922, **5**, 300-313.

A review of recent literature, several paragraphs of which are reproduced as abstracts in this number of Endocrinology.

—R. G. H.

An ENDOCRINAL factor in general paresis. Davis (T. K.), Am. J. M. Sc. (Philadelphia), 1922, **163**, 425-430.

Based upon the ideas that status lymphaticus can be used as an indication of hypoplasia of **adrenal** cortex and that trichosis in an individual can be used as a measure of suprarenal valence, the author reports upon 82 cases of general paresis which he has thus examined. His conclusions are: (1) The endocrinal status of the individual has a discernible influence in determining whether, once

infected with syphilis, he is likely to develop paresis; (2) status lymphaticus is rare among male paretics and is seen less frequently among paretics than among male hospital cases which come to autopsy; (3) individuals who have low suprarenal functioning appear to develop paresis less frequently than strong suprarenal individuals; (4) the course of general paresis on the average varies in rapidity directly with the suprarenal strength of the individual.
—J. F.

ENDOCRINE status and dynamism of gastro-crino-kinetic drugs. Duran (F.), Arch. di. farmacol. sper. (Roma), 1921, **31**, 135-142, 177-183.

Atropine diminishes the acidity and the digestive power of the gastric juice, while pilocarpine has the opposite effect. The endocrine preparations, **thyroglandol, pituoglandol, adrenalin** and pancreatin, increase the acidity without affecting the digestive power. **Suprarenal** preparations do not counteract the effect of either atropine or pilocarpine in these respects, while thyroid and pancreatic preparations inhibit both the decreased motility caused by atropine and the increased motility caused by cascara.—Chem. Abst., **16**, 439.

Neurasthenia as ENDOCRINE syndrome (La neurasthénie considérée comme un syndrome endocrine). Goormaghtigh (N.), Arch. méd. belges (Brux.), 1921, **74**, 1040-1045.

The article is an abbreviated translation of a recent article by Harrower.—R. G. H.

Constitution and the ENDOCRINE system (Konstitution und endokrines System). Hart (C.), Ztschr. f. ang. Anat. [etc.], (Berl.), 1920, **6**, 71-84.

A general article calling attention to the specific endocrine pattern of every individual whereby growth, development, form, psychic function and other manifestations of life are determined. Pathological conditions particularly mentioned as endocrinopathies are **status thymo-lymphaticus, infantilism, eunuchoidism** and **mongolism**. While status thymo-lymphaticus and infantilism may be inherited, the same symptoms may result from intra- or extra-uterine disturbances of the endocrine organs so that it is difficult to decide whether in a given case it is inherited or acquired. The author warns against the association of such anomalies with a particular ductless gland and believes it erroneous to explain infantilism as being due to hypofunction or disfunction of the thyroid. He also objects to classifying infantilism as **dysgenitalism**, maintaining that there is always a general involvement of the whole endocrine system. Regardless of the primary cause, or the particular ductless gland which is most affected, general involvement

of the endocrine system must also be recognized in the other three abnormalities mentioned above and possibly also in asthenia universalis. Just as the normal so the pathological pattern is under endocrine dominance. No bibliography.—A. T. R.

(ENDOCRINE GLANDS) Glandular dystrophies and particularly mono-symptomatic dystrophies (Dystrophies glandulaires et particulièrment dystrophies mono-symptomatiques). Hutinel (V.) & Maillet (M.), Ann. de méd. (Paris), 1921, **10**, 364-385.

A continuation of the discussion previously reported.—F. S. H.

(ENDOCRINE ORGANS) Atrophy of human organs in inanition (Über die Atrophie der menschlichen Organe bei Inanition). Krieger (Marie), Ztschr. f. ang. Anat. [etc.], (Berl.), 1920, **7**, 87-134.

The organ weights are given in 135 cases (in six groups as follows: I, 11 cases without chronic disease; II, 7 with chronic dysentery; III, 27 with malignant tumors; IV, 31 with chronic general infection; V, 40 with tuberculosis; VI, 19 various cases of senility) where the body had lost from 35.8 to 48.4 (average of each group). The **spleen** showed a loss of 46.6 per cent in group I, 36 per cent in group II, 27.6 per cent in group III, and 48 per cent in group VI. The **pancreas** showed a loss of 44.8 per cent in group II, 33 per cent in group III, 30.5 per cent in group IV, and 28.6 per cent in group V. The **thyroid** showed a loss of 47 per cent in group II, 20.6 per cent in group III, 32.3 per cent in group IV, and 35.8 per cent in group V. The **suprarenals** together showed a **gain** in weight in nearly all cases; the figures for the four groups where weights were taken being: Loss of 8.6 per cent (from his figures and not 17.2 as tabulated) in group II, gain of 21.5 per cent in group III, gain of 23.2 per cent in group IV, and a gain of 6.6 per cent in group V. The **testes** showed a loss of 41.3 per cent in group II, 28.7 per cent loss in group III, 40.3 per cent loss in group IV, and 49.4 per cent in group V. The **hypophysis** showed practically no change in weight although only 30 glands were weighed and these belonged to groups II, III, IV and V. Similar tables are given for the liver, heart, kidney and brain. These results are compared with the observations others have made on the cat, dog and pigeon. Eighteen cases are given in detail. Some references are given.

—A. T. R.

The interrelations of the ENDOCRINE ORGANS in Graves' disease, in diabetes and the rejuvenation problem (Die Wechselwirkungen der Blutdrüsen bei der Basedow'schen Krankheit, dem Diabetes mellitus und dem Verjüngungsproblem). Leschke (E.), Wien. med. Wchnschr. (Wien), 1921, **71**, 27-33.

According to Leschke, growing old, at least in the human subject, is caused not only by extinction of the function of the **interstitial** generative **glands**, but in a still greater degree by suppression of the function of the other glands of internal secretion, among which the anterior lobe of the **hypophysis** and the **suprarenal** cortex play the most important part. In attempting to produce an artificial rejuvenation in man Leschke endeavors to stimulate the suprarenals, **thyroid**, and hypophysis by x-rays, and does not confine himself to stimulating the generative glands by ligature of the vas deferens, irradiation of the **testes** or **ovaries**, or transplantation of portions of these organs. In the estimation of the results of supposed rejuvenation, Leschke recommends the exercise of considerable reserve, especially as one has to depend on the statements of patients who may have been influenced by the propaganda in the daily press.—Med. Sci., **5**, 310.

Glandes ENDOCRINES et syphilis fonctionnelle ou meiopragique. Merklen (P.), La Médecine (Par.), 1921, **2**, 774-776.

In a general discussion Merklen points out that syphilis may play a significant etiologic role in the pluriglandular endocrinopathies. Antiluetic treatment in such cases is important.—R. G. H.

(ENDOCRINE ORGANS) Etiology of post-war late rachitis (Spätrachitis in der Nachkriegszeit und Konstitution. Ein Beitrag zur Ätiologie der Erkrankung). Neuberger (H.), Ztschr., f. ang. Anat. [etc.] (Berl.), 1921, **8**, 15-41.

From an analysis of 38 (33 male and 5 female) patients from 12 to 20 years of age, it is concluded that disturbances of one or more ductless glands (**gonads, thyroid, parathyroids, thymus, hypophysis,** and perhaps also the **pineal** gland and **suprarenals**) are nearly always present in calcium deficiency diseases of the bones, such as rickets and osteomalacia; the proper functioning of the endocrine system being apparently necessary to normal calcium and phosphorus metabolism. Lack of vitamines may be a primary factor in producing this glandular disfunction. A short list of German references is given.—A. T. R.

The relations between the ENDOCRINE ORGANS and abnormalities of teeth and jaws (Die endokrinen Drüsen in ihrer Beziehung zu Zahn und Kieferanomalien). Petzel (W.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 231.

A good short review of the literature. No new data are adduced.—J. K.

Asthenias of ENDOCRINE origin (Le diagnostic des asthenies d' origine endocrinienne). Sézary (A.), Presse méd. (Par.), 1922, **30**, 79-81.

Sézary recalls that asthenia is common to innumerable diseases of totally different origin, and points out that an unfortunate tendency to blame the endocrine glands for every symptom is becoming prevalent. Although asthenia is doubtless the most frequent symptom of endocrine disturbances, and characteristic of Addison's disease in which histologic examination rarely fails to reveal **adrenal** lesions, anatomical findings do not support the conclusion that the asthenia of every endocrine syndrome is merely caused by adrenal insufficiency. Sézary recognizes two distinct types of asthenia which are both of endocrine origin. The first type is connected with adrenal lesions and combined with muscular weakness and extreme fatigability: it occurs in Addison's disease and in epinephrectomized animals; myasthenia would be the better term, as the muscle itself becomes exhausted and the symptoms correspond with the disease of that name (Erb and Goldflam's myasthenia). The second type does not furnish evidence of adrenal involvement at necropsy, although asthenia is present, and there is no increased muscular fatigability. These types can be distinguished by means of the dynamometer: the rapid muscular exhaustion of adrenal insufficiency gives a curve with sudden drop, the muscular weakness of other asthenic conditions shows a slowly declining curve, similar to that of muscular fatigue in normal persons. The test is of therapeutic value, for improvement can be obtained by administration of total adrenal substance when adrenal involvement is actually present, whereas little benefit results when the adrenals are not at fault. In the case of a woman confined to her bed for ten years by muscular weakness, such as to prevent her from standing for more than ten minutes at the time (a case of adiposis dolorosa) the dynamometer showed a gradual decline; suprarenal therapy caused but a slight, transient improvement, but **thyroid** medication accomplished a complete cure. In a case of tuberculous melodermia, with pigmentation even of the mucous membrane, the dynamometer did not register the sudden drop of muscular fatigability and necropsy revealed marked degeneration of the liver with intact adrenals. Erb and Goldflam's bulbar asthenia, is characterized by weakness of the oculomotor, facial and cervical muscles, followed by paralysis with demonstrable inflammatory lesions in the muscles; asthenia of adrenal origin does not show any predilection for the muscles enervated by cranial nerves and is not followed by paralysis. These examples show that not all myasthenias even are referable to adrenal insufficiency; they are presented with the object of furthering a more accurate classification of asthenic conditions of endocrine origin. Sézary states that he found adrenal lesions at necropsy in every case in which rapid muscular fatigability had been observed; he questions the existence of adrenal insufficiency when histologic examination fails

to reveal caseous degeneration, invading tumors, extensive necrosis or sclerosis of the adrenal glands.—G. L.

(GONADS) Hermaphroditismus spurius masculinus. Fröhlich, Berl. klin. Wchnschr., 1921, **58**, 1544.

The patient was a man of 18 with a complete male habitus but without erections or pollutions. The distribution of hair was completely male. The external sexual organs were very small; there was a hypospadias perineoscrotalis. Prostate and seminal vesicles could not be found. As a tumor was felt in the abdomen a laparotomy was carried out. The left sexual gland was enlarged and contained testicle as well as tumor tissue (epithelioma chorioectodermale). The right gland was replaced by an enormous tumor. It was attached to a ligamentum latum. On the right side a fallopian tube with fimbriae was found. There was no uterus.

—J. K.

(GONADS, BIDDER'S ORGAN) Investigation of Bidder's organ of male and female toads (Untersuchungen über das Biddersche Organ der männlichen und weiblichen Kröten. I. Mitteilung: Die Morphologie des Bidderschen Organes). Harms (W.), Ztschr. f. Anat. u. Entwicklungsgesch., (Berlin), 1921, **62**, 1-38.

The article deals with the general history, development and significance of Bidder's organs with special reference to the secondary sex characters, and the interstitial cells of the **testis** and **ovary** of the toad. In Bufo vulgaris the annual cycle of the ovary, testis and Bidder's organ in relation to the breeding habits is given in detail. In the male, Bidder's organ decreases one-half or even two-thirds of its original volume during and for two months after the breeding season; while in the female this organ acts just the reverse by increasing enormously during and for some time subsequent to the breeding season. The author maintains that the interstitial cells of the testis (which he regards as merely storage or transporting organs for products of the sex cells proper), the **lutein cells** of the **ovary** and the granulosa cells of Bidder's organ discharge their inclusions into the blood stream and thus affect the secondary sex characters. Animals with only Bidder's organ intact (concerning which he promises a second "Mitteilung"), the **testes** having been removed, show the usual secondary sex characteristics during the breeding season. Both gross and microscopic illustrations of the organ are included. An extensive list of references is given.—A. T. R.

(GONADS) Hermaphroditismus externus without internal genital organs. Holst (J.), Norsk. Mag. f. Laegevidensk (Kristiania), 1921, **82**, 177-181.

Holst reports one case: A person 21 years old who passed as a woman. She was well educated and intelligent, but did not know to what sex she belonged. She entered the hospital because of a large tumor in her lower abdomen. The external genitalia consisted of a penis or clitoris 4 cm. long, at the base of which was the urethral opening so situated as to form a pronounced hypospadias. Posterior to the "penis" were two skin folds simulating the labia majora. The labia minora were absent. About 2 cm. below the urethral orifice was the opening of a 5 cm. canal, the lumen of which admitted the point of a pencil. This extended upwards and backwards to end blindly near the rectum. There was no evidence of either scrotum or testicles and the inguinal canals were empty. The tumor, removed by operation, was about the size of a man's head. It filled the true pelvis and was attached by two broad pedicles to the region of the ovaries. Symmetrically placed on the tumor were two structures that looked somewhat similar to Fallopian tubes; microscopically they also resembled tubes. A most careful macroscopic and microscopic examination failed to reveal any other sign of internal genital organs. The patient recovered from the operation. The first microscopic diagnosis made was adenocarcinoma from ovarian epithelium, but Holst is inclined to consider the new growth a teratoma containing only one type of tumor tissue.

As to secondary sexual characteristics: The voice had the timber of an adolescent male; there was some beard present, and the mammary glands were too small for a female and too large for a male.—D. J. G.

Morphology of the female GONADS in the domestic animals (Beiträge zur Morphologie der weiblichen Geschlectsorgane bei den Säugetieren). Küpfer (M.), Vrtljschr. d. naturf. Gesellsch. in Zurich, 1920, **65**, 377-433; Abst., Schweiz. med. Wchnschr. (Basel), 1921, **51**, 984.

In a great mass of material Küpfer studied the evolution of the corpus luteum. Both evolution and devolution were found to be regular. At each ovulation there developed from the ruptured follicle a corpus luteum, which, after it had reached its full development, retrogressed. An intervolution period was thereby delimnated which, in cows, lasted 31 days. In the intervolution period the evolution of the corpus luteum took place, while at the same time a new Graafian follicle developed. The intervolution period was ordinarily related to ovluation but did not regularly synchronize with the rutting period. Ovulation was apparently not determined in any way by copulation. Uterine hemorrhage which did not invariably occur was likewise not definitely related to rutting and ovulation.—R. G. H.

(GONADS) Specific actions of sex hormones and embryonal asexuality (L'action spécifique de la sécrétion interne des glandes sexuelles et l'hypothèse de l'asexualite de la forme embryonnaire). Lipschütz (A.), Rev. Scient. (Par.), 1921, — — (No. 1), Reprint 15 p.

The author emphasizes the fact that though interstitial cells may be absent in batrachians and birds, they constitute a well marked endocrin gland in mammals. Whatever may be said as to the intrinsic sexuality of the fertilized ovum, the gonadal hormones play an important rôle in the efflorescence of the sexual characteristics. The paper, being itself largely a summary, should be consulted for details in the original.—R. G. H.

(GONADS) Eunuchoidism in the rabbit, with the presence of spermatozoa in the canaliculi and with defective interstitial cells (Ueber Eunuchoidismus beim Kaninchen in Gegenwart von Spermatozoen in den Hodenkanälchen und unterentwickelten Zwischenzellen). Lipschütz (A.), Bormann (T.) & Wagner (K.), Deutsche med. Wchnschr. (Berl. & Leipz.), 1922, **48**, 320-322.

The authors observed a rabbit with eunuchoid habitus, many spermatozoa in the testicles and poorly developed interstitial cells. The penis was very small. In a second animal of the same litter puberty was retarded; spermatozoa were also present, but the interstitial cells were small. Therefore, the authors agree with Steinach that the interstitial cells are the puberty glands, and that the seminal cells have no influence on the secondary sexual characteristics.—J. K.

(GONADS) Dysgenitalism in two brothers (Dysgenitalismus bei zwei Brüdern). Mayer (C.), Wien. klin. Wchnschr. 1922, **35**, 118.

Two brothers of 26 and 24 years, respectively, showed a typical eunuchoid habitus. Each had the penis and testicles of a small child, no beard, no axillary hairs and a sella turcica of normal size. Only the elder brother had pubic hair. Both were very intelligent; both had enlarged tonsils. One of them had a small goiter.—J. K.

(GONADS) The psychopathology of puberty and adolescence. The Morison Lectures for 1921. Mott (F.), J. Ment. Sc. (Lond.), 1921. **The second Maudsley Lecture, 1921.** Mott (F.), J. Ment. Sc. (Lond.), 1921.

In these four lectures are included, among much varied and interesting material, the results of Mott's prolonged and original observations on the morbid lesions in the testis and ovary in both germinal and acquired mental disease. The present abstract refers

to this work alone. In dementia praecox, Mott finds that the testis undergoes regressive atrophy, which, according to the duration of the disease, varies from the slightest morphological and biochemical changes to total atrophy of the seminiferous tubules and cessation of spermatogenesis. Speaking generally, he finds that the earlier the onset of symptoms and the longer the duration of life subsequently, the more complete the atrophy. Even the testis of a man of 80 years showed much clearer signs of functional activity. On the other hand, in such an acquired form of mental disease as dementia paralytica, the atrophic changes are focal, and side by side by areas of ovary from cases of dementia praecox shows changes of the same order. To the naked eye the organ is smaller and lighter than normal and has a crinkled appearance. This is true even when the patient has had a child, and such patients appear rarely to have more than one. Microscopically, there is no evidence of recently matured Graafian follicles. The continuous zone of primordial follicles normally found in early life is absent in this disease. Such small follicles as are present show evidence of degeneration. Such regressive atrophy is not found in dementia paralytica. The critical periods of life as regards mental disease, Mott believes to be adolescence and the climacteric, that is, when the sexual function becomes mature and wanes, respectively. He believes this to indicate important relations between sexual functions and mental disease. Discussing the question whether the atrophy of the sexual organs is the cause or an accompaniment of the mental symptoms, he concludes that there is a germinal-biochemical failure of all nuclear material in the body, but of that of the central nervous system and sexual organs particularly, with a corresponding defect of reproductive and "psycho-physical" energy. This failure in many cases begins before puberty. Turning then to the essential lesion of the nervous system in dementia praecox, Mott concludes, from his own observations and those of Nissl, Alzheimer, and others, that this consists in a parenchymatous degeneration of the neurones, with relatively little morbid change in the mesodermic supporting tissues. The histological peculiarities of the affected neurones are described at length, and Mott concludes that a failure of oxidation processes dependent upon a defect of the vital energy of the nucleus underlies the mental manifestations. A similar failure accounts for the regressive changes seen in the sexual organs. An admirable series of drawings illustrated the series of lectures.—Med. Sci., **5**, 332-333.

(GONADS) Castration of hen-feathered Campines. Morgan (T. H.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17**, 70.

See Endocrinology **4**, 381-385.

(GONADS) Vasectomy practiced on a dog with a view to rejuvenation (Vasectomie pratiquée chez un chien dans un but de régénération). Sand (K.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1201-1205.

The author gives a full description of the results of a bilateral vasectomy on a decrepid dog, over twelve years of age, done with the aim of rejuvenating the animal. The operation, a vasectomy on the left side, a resection of the epididymis on the right, was done May 23, 1921. After a few weeks the dog began to improve. Nutrition was nearly normal, the force and tonus of the muscles was satisfactory. He preceded a bicycle going at a rate of 15 km. per hour. The skin was supple, and the hair was smooth and shiny. He walked with a free gait and held his head high. He again showed interest in the female and had coitus on November 20th. The animal seemed full of life.—T. C. B.

(GONADS) Internal secretion and especially Steinach's rejuvenation (Ueber innere Sekretion, speziell über die Steinachschen Verjüngungsversuche). Schmidtgen & Gruber, Berl. klin. Wchnschr., 1921, **58**, 1547-1548.

Steinach's rejuvenation is not a real rejuvenation but only a return of sexual desires. Though the experiments of Steinach are highly interesting there has been as yet no justification established for carrying out his operation in man. It has not been proved that an animal lives longer after Steinach's operation than it would have done without it.—J. K.

Development, structure and significance of the interstitial cells of the GONADS (Entwickelung, Bau und Bedeutung der Keimdrüsenzwischenzellen). Stieve (H.), Ergebn. d. Anat. u. Entwicklngsgesch. (Wiesb.), 1921, **23**, 1-249.

An extensive and critical review of the literature with special reference to the endocrine function of the ovary and testis. Nearly 1,000 references are listed. No new data are added.—A. T. R.

(GONADS) The effects of ligation of the vas deferens (Over gevolgen van vas deferens onderbinding). de Vrieze (T. J.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, 66 (I), 266-281.

A man of 63 suffered from vomiting, constipation and want of appetite. He also had hypertrophy of the prostate. The patient was energetic and vigorous. A ligation of both vasa deferentia was made because of the hypertrophy of the prostate. After this the patient became extremely quiet, did not leave his bed any more, had no appetite at all, had no interest in anything. He died of cachexia. Autopsy showed hypertrophy of the prostate, cystitis and purulent

pyelonephritis. The testicles were atrophic without spermatogenesis. There was no increase in the number of interstitial cells. This is the first case of this operation with a report of a post-mortem examination.—J. K.

Diabetes insipidus and HYPOPHYSEAL INFANTILISM (Diabete insipido ed infantilismo di origine ipofisaria). Antonelli (G.), Policlin. (Roma), 1920, **27,** 1203-1210, Sez. Prat.

According to Antonelli, who records an illustrative case, Strauss in 1912 was the first to draw attention to the relation between diabetes insipidus and arrest of development,and cases of this kind have since been reported by Ebstein, Kopezynski, Lereboullet, Faure-Beaulieu and Vaucher, and Souques and Chauvet. In Antonelli's case, which occurred in a man aged 23, in whom arrest of development occurred at 13, pituitary involvement was shown by intense polyuria, attacks of headache and giddiness, asthenia, optic atrophy, bitemporal hemianopsia, low blood-pressure, and somnolence. In the absence of an autopsy the nature of the pituitary lesion could not be determined, but in view of the long history it was probably a benign tumour.—Med. Sci., **5,** 398-399.

Autoplastic transplants of the epithelial HYPOPHYSIS in larvae of Rana pipiens. Atwell (W.), Anat. Record (Phila.), 1922, **23,** 8.

The epithelial hypophysisis was transplanted from the head to the tail in very young tadpoles. The experimental animals failed to develop the typical silvery appearance of the hypophysectomized tadpole. They were, however, lighter in color than normal larvae. Examination of the living tadpole under the binocular microscope showed that the melanophores were not so contracted nor the xantholeucophores so widely expanded as in the typical silvery larva. The hypophysis, or at least the pars intermedia—which is responsible for the color change—had been only partly compensated for by the transplant. The condition is evidently that of a chronic hypophyseal insufficiency.—Author's abst.

(HYPOPHYSIS) Obesity in essential hydrocephalus (L'obésité dans l'hydrocephalie essentielle). Babonneix (L.) & Denoyelle (L.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46,** 150-158.

A case report and review of the literature, the conclusion of which is that essential hydrocephalus can be complicated by obesity in certain cases. This obesity seems to be produced by an interesting lesion, not of the hypophysis, but of the infundibulum or the epiphysis.—F. S. H.

Radium treatment of HYPOPHYSEAL tumor in acromegalic syndrome (Radiumterapia dei tumori ipofisarî a sindrome acromegalica). Bertolotti (M.), Gior. d. r. Accad. di med. di Torino, 1920, **83,** 110-122.

Bertolotti records the case of a man, aged 35, who was admitted to hospital with all the signs of a rapid and malignant attack of acromegaly, viz., almost complete blindness, profound adnyamia, sexual impotence, and advanced cachexia. X-rays showed a pituitary tumor the size of a small nut compressing the chiasma. The patient was subjected to radium treatment amounting in all to 7,360 mgm., distributed over eight seances in the course of four months, There was at first an aggravation of all the symptoms, but after about a month slow but progressive improvement set in, and finally a permanent clinical cure was established.—Med. Sci., **5**, 309-310.

(HYPOPHYSIS) Dystrophia adiposogenitalis. Böge, München. med. Wchnschr., 1921, **68**, 1668.

This article describes a man of 24 with feminine habitus, macrosomia, adiposity, hypogenitalism, and defective development of the bones. The cause is perhaps a change of the pars anterior of the hypophysis. On the x-ray plate there is a shadow (tuberculoma?) in the place of the pars anterior.—J. K.

(HYPOPHYSIS) The anencephalic syndrome in its relation to apituitarism. Browne (F. J.), Edinb. M. J., 1920, N. S., **25**, 296-307.

From the examination of five anencephalic monsters, Browne has come to the conclusion that the characteristic physical signs of anencephaly, apart from the absence of the brain and cranial vault, are connected with absence of the pituitary gland. These characteristic physical signs are as follows: (1) maldevelopment of the basis cranii; (2) protruding eyeballs; (3) protruding tongue; (4) aquilinity of nose; (5) large amount of cutaneous fat; (6) hyperplasia of the **thymus**; (7) small or absent **suprarenal** gland; (8) hyperplasia of the **genital organs**; (9) stunted growth of the trunk and limbs. Browne maintains that the internal secretions of the mother play no part, or at least a very minor one, in the development of the foetus, as they seem to have no effect in compensating for the secretions that are wanting in anencephaly. It is evident, also, that the endocrine glands of the foetus play an extremely important part in its development in utero.—Med. Sci., **5**, 307.

Oxytocic influence of extracts of HYPOPHYSIS and a new remedy, "Physormon" (Ueber die Art der Wehenanregung durch Hypophysenextrakte und über das neue Mittel Physormon). Calmann (A.), Zentralbl. f. Gyn. (Leipzig), 1921, **45**, 1841-1842.

The author tried unsuccessfully to initiate labor by the use of extract of hypophysis as recommended by Steig. However, excellent results were obtained when repeated injections in extremely small doses were made. "Physormon" is a preparation made from

the pars posterior and intermedia of the hypophysis. It seems to be very active and may be used as a styptic as well as in amenorrhea. Also in urinary retention and in paralysis of the bowels it seems to have a good effect. It produces a very marked rise of blood pressure.—J. K.

A case of tumor of the HYPOPHYSIS (Een geval van hypophysisgezwel). Carp (E. A. D. E.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1921, **66** (I), 350.

The case is reported of a man of 33 who complained of bad vision and headaches, without vomiting. He felt drowsy. There was beginning adiposity, loss of sexual desires, and loss of hair, but no polyuria or increased sugar-tolerance. Blood examination showed slight relative and absolute lymphocytosis. An enlarged sella turcica with changes in the dorsum sellae was apparent on the x-ray plate.—J. K.

(HYPHOPHYSIS) A case of pluriglandular insufficiency with acromegaly (Un cas d'insuffisance pluriglandulaire avec acromégalie). Caussimon (J.), J. de méd. de Bordeaux, 1920, **91**, 462-465.

Caussimon, of Bordeaux, reports a case of acromegaly in a woman aged 36, associated with signs of pluriglandular insufficiency, viz., symptoms attributable to the **thymus, thyroid,** and **ovary.** There was no enlargement or deformity of the sella turcica on x-ray examination. Out of 33 cases of acromegaly collected by Caussimon from the literature between 1886 and 1919, in 26 no mention is made of persistence of the thymus, in 4 the presence of characteristic retrosternal dullness is noted, in 2 a persistent thymus was found, and in one no trace of it was present post-mortem. The thyroid in these cases was sometimes atrophied and sometimes enlarged. Occasionally there was exophthalmos. In the present case there was definite atrophy of the thyroid, and the development of the subcutaneous tissue, appearance and texture of the skin, and scantiness of hair resembled those in myxoedema. Disturbance of the ovarian function was shown by amenorrhoea which had been present from the onset, as in 30 of the 33 collected cases. The present case did not show any symptoms attributable to the **suprarenals,** and in only two of the 33 cases was involvement of these glands noted. Thus Motais states that his patient's skin became bronzed as in Addison's disease, and Gilbert Ballet and Laignel-Lavastine's case the suprarenals were found post-mortem to be full of adenomas.—Med. Sci., **5**, 309.

(HYPOPHYSIS) Defects in membranous bones, exophthalmos and diabetes insipidus: an unusual syndrome of dyspituitarism. Christian (H. A.), Med. Clin. N. Am. (Phila.), 1920, **3**, 849-870.

Christian, of Boston, records the case of a girl, aged 5, who presented the symptom-complex of diabetes insipidus associated with very extensive defects in the skull-bones and bilateral exophthalmos. Pituitary extract controlled the polyuria when given subcutaneously, but no other method of introducing pituitary substance had any effect upon the polyuria, and no method of giving pituitary substance had any influence on the bone defects or the exophthalmos. Only two similar cases have been recorded, viz., by Schüller, of Vienna, who, in a subsequent paper in which he comments on Christian's case, comes to the conclusion that the syndrome is due to disease of the hypophysis, like acromegaly, dystrophia, adiposogenitalis, and pituitary dwarfism.—Med. Sci., **5**, 399.

La pathologie du naso-pharynx et des sinus sphènoïdaux contribue a la pathologie du système HYPOPHYSAIRE. Citelli, L'oto-rhino-laryngologie internationale (Lyon), 1919, Reprint, 5 p.

Citelli summarizes the work of himself and his pupils on the significance of the pharyngeal hypophysis. He believes that it is a functionating organ that shares in the activity of the hypophysis, proper, with which it is not infrequently connected by a persistent pharyngo-hypophyseal duct. Evidence is cited that the "hypophyseal system" may be affected by nasopharyngeal or sphenoidal sinus disease giving rise to a syndrome marked by mental sluggishness. This is frequently ameliorated by hypophyseal medication.

—R. G. H.

On the PITUITARY active principles and histamine. Dale (H. H.) & Dudley (H. W.), J. Pharmacol. & Exper. Ther. (Balt.), 1921, **18**, 27-42

These investigators agree with Abel and Nagayama that boiling with 0.5 per cent HCl destroys the pressor and oxytocic actions of pituitary extract. However, they find that the oxytocic substance is not completely destroyed by six hours' boiling. Moreover, the oxytocic action obtained from the substance remaining is much greater than that from histamine of equal depressor action. They see no reason to suggest a relation between histamine and the specific action of the extract. The specific oxytocic principle is slowly destroyed by erepsin.—F. A. H.

Characteristic effects upon growth, oestrus, and ovulation induced by the intraperitoneal administration of fresh anterior HYPOPHYSEAL substance. Evans (H). & Long (J.), Anat. Record (Phila.), 1922, **23**, 19.

Daily intraperitoneal injection of fresh anterior lobe of beef hypophysis causes acceleration of growth in white rats. Oral administration fails to do this. Oestrus may never occur or may be

exhibited only at long intervals. **Ovaries** were always enlarged, showing much **lutein** tissue about unruptured normal follicles and atretic follicles. Ripe, normal Graafian follicles were invariably absent.—W. J. A.

The secretory activity of the anterior lobe of the PITUITARY body during pregnancy (Sull'attività secretiva della preipofisi in gravidanza). Gentili (A.), Sperimentale; Arch. di biol. (Firenze), 1920, **74**, 286-291.

Investigations were carried out by means of over 100 pituitary bodies collected from cows at different periods of pregnancy, as well as on many specimens from nulliparous animals. The results obtained are in great part a confirmation of well known facts, and may be summarized as follows: The anterior lobe of the pituitary body increases progressively in size and weight from the beginning to the end of pregnancy. While the average weight of the hypophysis of nulliparous cows is from 135-140 mgm., it already reaches 170 mgm. at the beginning of a first pregnancy, increasing up to 350 mgm. at the end of it. In cows of the same body weight, but multiparous, the weight of the pituitary body may increase from 310 up to 460 mgm. This means that in proportion to the body weight that of the hypophysis grows from 1:100,000 in nulliparous cows to 1:50,000 at the end of the pregnancy in multiparous animals. Histologically the anterior lobe of the pituitary body of pregnant cows forms an excellent material for the study of the so-called gravidic cells, the chief function of which appears to be the secretion of a progressively increasing amount of lipoid substances, belonging, according to the author, to the phosphatides. Another feature of the anterior lobe of the pituitary body during pregnancy is the production of great quantities of colloid material, with the secretion of which the chromophobe cells appear to be chiefly concerned.—Med. Sci. **4**, 371.

(HYPOPHYSIS) The pathology of dystrophia adiposo-genitalis (Die Pathologie der Dystrophia adiposogenitalis). Gottlieb (K.), Ergebn. d. allgem. Path. u. path. Anat. [etc.], (Wiesb.), 1921, **19**, 575-650.

The author reviews both the clinical and the experimental work on dystrophia adiposo-genitalis. To study its pathogenesis in man he assembles from the literature the 87 cases in which autopsy findings are given, showing: (1) Some disturbance in or in the region of the hypophysis; (2) adiposity; (3) usually genital atrophy. From the analysis of these he concludes that the disease is due to an alteration or diminution in the hypophyseal secretion reaching the subthalamic centers. Tumors, cysts or other pathological changes involving the whole gland or one of its lobes, also

external pressure from a neighboring tumor or from hydrocephalus may be the cause. He looks upon adiposity as an effect secondary to the alteration in the carbohydrate metabolism. The usual cases of complete destruction of the hypophysis without dystrophy he is unable to explain. A bibliography of 159 complete references is given.—(D. M.) W. J. M. S.

(HYPOPHYSIS) Pathological anatomy and pathogenesis of dystrophia adiposo-genitalis (Zur pathologischen Anatomie und Pathogenese der Dystrophia adiposo-genitalis). Gottlieb (K.), Ztschr. f. ang. Anat. [etc.], (Berl.), 1920, **7**, 60-86.

The clinical and detailed autopsy findings in three cases of dystrophia adiposo-genitalis and a short summary of nine other cases are compared with cases recorded by others with the following conclusions: The clinical picture in dystrophia adiposo-genitalis is primarily due to involvement of the hypophysis. The disturbance of the hypophysis may be due to some extrinsic cause, such as tumors, hydrocephalus, etc., as well as to some primary pathological change in the hypophysis itself. The association of the disease with a particular lobe of the hypophysis is not justified, for it may arise from dysfunction of the anterior lobe as well as from interference with the discharge of the secretion from the posterior lobe and the stalk. Both hypo-secretion and abnormal (false) secretion as a rule result in dystrophia adiposo-genitalis, unless the false secretion arises from an acidophilic change in the anterior lobe, in which case acromegly results. If the hypophysis undergoes great damage in early childhood, **dwarfism** results. There are a few cases in which no disease results in spite of these pathological conditions. Such exceptions are explained upon the assumption that there is a hypo-sensitiveness in these individuals to the hypophyseal hormone or there is but little dependence of the central nervous system on pituitary influence. Fifty-five references to literature are given.

—A. T. R.

Action of the HYPOPHYSIS on growth (Action de l'hypophyse sur la croissance). Houssay (B. A.) & Hug (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1215-1218.

Observations have been made on twelve lots of young dogs (5-10 dogs to a lot) since 1908. Careful controls were kept; some were operated upon without the removal of the hypophysis and others left normal. "Young dogs deprived of the hypophysis present a dystrophy which is not due to operative traumatism, and which is characterized by arrest of growth, adiposity, change in character, modification of the genital organs, thyroid and thymus."

—T. C. B.

Meningeal relations of HYPOPHYSIS CEREBRI. Hughson (W.), Anat. Record (Phila.), 1922, **23**, 21.

Study of serial sections of this region shows that in addition to the dural covering of the floor of the sella turcica, the hypophysis is completely surrounded by an arachnoid membrane continuous with that of the brain. Similarly the pia is reflected upon the hypophysis investing it closely. Between these two membranes is a space, traversed by many trabeculae so that it becomes close-meshed. The continuity of this leptomeningeal space about the hypophysis with the cranial subarachnoid space has been demonstrated by two methods of injection.—Author's abst.

Adiposo-genital syndrome with HYPOPHYSIS tumors (Le syndrome adiposo-génital dans les tumeurs de l'hypophyse). Lereboullet, Progrès méd. (Par.), 1922, **37**, 52-55.

Lereboullet reviews the current evidence on the symptomatology, etiology and treatment of Fröhlich's syndrome.—R. G. H.

Tardy infantilism in the adult of HYPOPHYSEAL origin (L'infantilisme tardif de l'adulte d'origine hypophysaire). Lereboullet (P.) & Mouzon (J.), Paris méd., 1920, ii, 277-282.

According to Lereboullet and Mouzon, tardy infantilism in the adult of pituitary origin, which was first described by Gandy in 1906, is characterized by the loss of **sexual** characters of adult life, viz., loss of sexual function and morphological retrogression of the primary and secondary sexual attributes. The syndrome occurs during the height of genital activity between 20 and 40, and particularly between 30 and 35. The accessory symptoms which are usually present, according to Gandy, are: (1) some characteristics of **myxedema**, such as swelling of the face, dry and ichthyotic skin, and partial or total loss of hair: (2) headache, sweating, polydipsia and polyuria, which often mask the onset of the symptoms; (3) **gynecomastia**; (4) smallness of the **thyroid** on palpation; (5) a previous history of syphilis. The syndrome is generally produced by a pituitary lesion, which may be due to adjacent bony lesions.—Med. Sci., **5**, 307.

(HYPHOPHYSIS) Incipient acromegaly in infancy (Uber das Vorkommen von Akromegalie im Kindesalter). Petényi (G.) & Jankovich (L.), Monatschr. f. Kinderh. (Leipz. & Wien), 1921, **21**, 14-21.

Petényi and Jankovich record a fatal case of incipient acromegaly in a boy, aged 10½, who presented the characteristic facial appearance and thickening of the phalanges, though all the other typical symptoms of acromegaly, including psychical changes, were absent. Death was due to tuberculous meningitis. The autopsy

showed enlargement of the hypophysis, hyperemia of the anterior lobe, much increase in the eosinophil cells, and colloid change in the middle lobe. All the other **endocrine glands** presented a normal appearance, both on naked eye and on microscopical examination.—Med. Sci., **5**, 308.

Traumatic lesion of the HYPOPHYSIS and multiple paralysis of the cranial nerves (Lésions traumatiques de l'hypophyse et paralysies multiples des nerfs craniens). Reverchon (L.), Worms (G.) & Rouquier, Presse méd. (Par.), 1921, **29**, 742-743.

The authors report a fatal case of fracture of the base complicated not only by paralysis of several cranial nerves (V, VI, and VII), but also by **diabetes insipidus** (polydipsia and polyuria), intense anaemia and asthenia, low blood-pressure, **puerilism**, and apathy. The autopsy showed that the condition was due to severe lesions of the hypophysis, which was reduced to a small fibrous nodule in which no trace of normal tissue could be found on histological examination. The case suggests that the hypophysis is injured more frequently than is supposed in fractures of the base, either directly or indirectly, by compression by hemorrhage. The writers recommend that in fractures of the base one should look for evidence of diabetes insipidus as well as for the well-known signs accompanying this accident. X-rays will be of value in showing lesions of the posterior wall of the sella turcica.—Med. Sci., **5**, 398.

HYPOPHYSEAL cachexia due to acquired syphilis with cure (Uber hypophysäre Kachexie auf Basis von Lues acquisita mit Ausgang in Heilung). Reye, Med. Klin. (Berl. & Wien), 1920, **16**, 1313-1314.

Reye remarks that in addition to the two well-known types of pituitary disease, viz., acromegaly and dystrophia adiposo-genitalis, there is a third type which has been described by Simmonds, of Hamburg, under the name of cachexia of pituitary origin. It is characterized by severe cachexia with atrophy of all the organs, loss of teeth, eyebrows, eyelashes, axillary and pubic hair, as well as by psychical disturbance. This form of cachexia is caused by necrosis of the anterior lobe of the hypophysis, resulting from embolic processes occurring in the puerperium, and less frequently by malignant tumors or tuberculosis. Reye reports a case in a woman, aged 50, in whom the condition was due to acquired syphilis and was cured by antisyphilitic treatment. This is the first case on record in which pituitary cachexia was due to syphilis. In the seven other published cases of syphilis of the hypophysis (in six, congenital syphilis and in one, acquired syphilis) the clinical picture was that of dystrophia adiposo-genitalis.—Med. Sci., **5**, 307.

(HYPOPHYSIS) On the relative amounts of depressor and broncho-constrictor substance obtainable from the anterior and posterior lobes of the fresh pituitary gland. Roca (J.), J. Pharmacol. & Exper. Ther. (Balt.), 1921, **18**, 1-25.

A blood-pressure lowering and broncho-constrictor substance was obtained from the posterior and anterior lobes of the pituitary gland by treatment with mercuric chloride in HCl. By this method the pressor substance was removed. The posterior lobe furnished seven to eight times as much depressor substance as an equal weight of anterior lobe. A similar but somewhat greater ratio of the bronchoconstrictor substance was found in the two lobes. Chloroform dissolves from suitably prepared material a substance acting like histamine on the arterial pressure, uterus and bronchi. Chloroform takes up about twenty times more of this substance from the posterior lobe than from the anterior lobe, weight for weight. The chloroform-soluble substance was thought to be histamine.—F. A. H.

The effects of PITUITARY extracts on the body temperature of animals rendered poikilothermous by destruction of the optic thalamus. Rogers (F. T.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **19**, 125-127.

A series of pigeons was reduced to the poikilothermous condition by cauterization of the thalamus. After death absence of any gross visible changes in the hypophysis was confirmed. The organ in each of these animals had a perfectly normal appearance, although there may have been circulatory alterations or cytological changes invisible to the naked eye. The injection intra-peritoneally of from 0.2 to 1.0 cc. of pituitary extract (posterior lobe—Lilly) caused a sharp rise in body temperature. Injection of the extract into normal birds causes no temperature reaction greater than the range of the diurnal variations. In the poikilothermous pigeon the body temperature of which was artificially maintained at a normal level by keeping in a warm incubator, injection of pituitary extract was followed by a rise in temperature such as to threaten heat prostration. The rise in body temperature persisted for twelve to twenty-four hours and then fell to a level determined by the environmental temperature. The authors were unable to maintain the body temperature at the normal level by pituitary extract alone without the aid of the continuously warm incubator. Frequently repeated injections of the extract led to the death of the animal, preceded by weakness and general prostration. A number of quite different factors seem to be involved in this thermic reaction. Further details and discussion will be presented later.—R. G. H.

Ocular symptoms in syphilitic HYPOPHYSEAL disease. de Schweinitz (G. E.), Arch. Ophth., N. Y., 1921, **50**, 203-217.

De Schweinitz describes the ocular symptoms of hypophyseal disease in syphilitic subjects. He recognizes three groups of the disease. The first includes non-syphilitic pituitary disease in syphilitic persons. In the second the pituitary lesion is itself syphilitic. In the third group the hypophyseal disease occurs in the subjects of doubtful syphilis. The following case illustrates the first group. A man, aged 49 years, had demonstrable syphilis, with fine chorioidal changes. He suffered also from pituitary disease, as shown by the skiagraphic appearances of the sella turcica and bitemporal color hemianopsia. He complained of bad sight, headache and diplopia. Exophthalmos was present, as well as paralysis of the right external rectus and convergent squint. Sellar decompression, followed by the exhibition of pituitary body extract and specific treatment, resulted in considerable improvement. A second case was that of a man of 45, with a history of a primary syphilitic sore, who complained of diplopia and failing vision. There was paresis of the right external rectus and convergent strabismus. The field showed temporal color hemianopsia and other changes. Energetic specific treatment met with a prompt and satisfactory response. Later the patient neglected his treatment and had a relapse. On resuming treatment the result was satisfactory. In this case the pituitary lesion was itself syphilitic. The cases are also described of three women, who suffered from hypophyseal disease and were the subjects of doubtful syphilis. They were all treated with **thyroid** extract and pituitary body extract and with inunction of mercurial ointment. The results were good. The combination of these three agents appears to be a valuable one.—Med. J., Australia, 1921, ii, 356.

The effect of intraperitoneal injection of fresh anterior lobe substances in HYPOPHYSECTOMIZED tadpoles. Smith (P. E.) & Smith (I. P.), Anat. Record (Phila.), 1922, **23**, 38.

Intraperitoneal administration of anterior hypophyseal substance has been found more effective in restoring the normal conditions in the pigmentary and endocrine systems and in the growth rate than administration by mouth.—W. J. A.

Transplantation of the pars nervosa of the PITUITARY. Swingle (W. W.), Anat. Record (Phila.), 1922, **23**, 125.

Subcutaneous homoplastic and heteroplastic transplantation of the pars nervosa of adult Rana clamata and R. catesbeiana into larvae causes shrinkage and emaciation after twelve hours. Control grafts of the pars anterior and brain tissue show no such effect. It is held that the shrinkage is due to the stimulation of the mesonephros to increased elimination of water.—W. J. A.

(HYPOPHYSIS) Traumatic diabetes insipidus, successfully treated with pituglandol (Diabetes insipidus nach Trauma, erfolgreich mit Pituglandol behandelt). Thörner (W.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 280-282.

A man fell out of his aeroplane from a height of 500 meters, causing commotio cerebri without fracture of the skull. After some days, polyuria and polydipsia were observed. The blood had a high specific gravity (1064) with many erythrocytes (6,600,000) and hyperlymphocytosis. The sugar tolerance was high and after injection of adrenalin, no glucosuria was seen. Repeated injections of adrenalin slightly diminished the daily quantity of urine, but did not produce a rise of blood pressure. Injections of pituglandol diminished the quantity of urine, though the concentration stayed low. The blood became normal.—J. K.

The influence of feeding anterior lobe of HYPOPHYSIS on growth and size of Amblystoma tigrinum. Uhlenhuth (E.), Anat. Record (Phila.), 1922, **23**, 43.

The author states that anterior lobe substance, when fed to metamorphosed Amblystoma tigrinum, causes an increase in the rate of growth and size, the animals becoming larger than those fed on other substances.—W. J. A.

The influence of feeding the anterior lobe of the HYPOPHYSIS on the size of Amblystoma tigrinum. Uhlenhuth (E.), J. Gen. Physiol. (Balt.), 1922, **4**, 321-330.

Amblystoma tigrinum fed on hypophysis of cattle grew much more rapidly than those fed on earth-worm, even up to 132 weeks. The feeding of beef-liver as compared with hypophysis produces equally rapid growth but growth ceases much earlier.—M. E. C.

Over INFANTILISME. de Vries (E.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66**, (I), 349.

The author discusses the case of a girl of 17 with dwarfism, adiposity and a very defective development of the sex characteristics. Only the skeleton is of the female type. The girl is idiotic. No other details are given.—J. K.

Action of INTERNAL SECRETIONS on the iris. Mazzei (A.), Arch. di ottal., 1918; Klin. Monatsbl. f. Augenh., 1919, **62**, 838-; Zentralbl. Biochem. Biophys., **21**, 396-.

Mazzei describes experiments with freshly enucleated frog eyes, one of which was placed in Ringer solution and the other in Ringer solution containing the substance to be tested. **Adrenaline, ovarin, endohypophysin** and **endothyreoidin** caused dilatation of the pupil (most rapidly with adrenaline and most slowly with endothyreoidin).

Spermin caused rather prompt contraction of the pupil. In the case of simultaneous action of various hormones those with mydriatic effect usually acted less rapidly than those with myotic effect, e. g., 5 drops of a mydriatic extract plus 3 drops of spermin caused slight myosis during the first few seconds, and this was followed by mydriasis after a few minutes. The slight myotic effect of spermin was inhibited by adrenaline, ovarin, thyreoidin and hypophysin and seldom had a predominant influence under such conditions.—Chem. Abst. **14**, 34.

Pernicious anemia and INTERNAL SECRETION (Perniziöse Anämia, Konstitution und innere Sekretion). Schauman (O.), Ztschr. f. ang. Anat. [etc.] (Berl.), 1920, **6**, 258-288.

The author maintains that the idea that pernicious anemia has as a basis certain constitutional anomalies, is becoming more generally accepted. The literature and a few cases of his own are analyzed from this point of view. He concludes that at the bottom of pernicious anemia are anomalies of the endocrine system as well as of the bone marrow. For example, the thinks it not unreasonable to consider that the pigmentation is due to functional or structural changes in the **suprarenals** or **chromaffin system.** Individual differences in the clinical picture are considered to be due not only to differences in the external exciting cause, but also the variability in the inherent ductless gland pattern of the individual. Some of the factors, those which are responsible for the blood changes, are always present; others, such as those responsible for achylia, are less regularly present; while still others (those responsible for renal disease, spinal cord symptoms, abnormal pigmentation, psychic disturbances, cardiac hypertrophy, abnormal pigmentation, etc.) are only occasionally in evidence. An extensive list of references is given.

—A. T. R.

(MAMMA) Mastitis adolescentium [Zur Frage der akuten schmerzhaften Brustdrüsenschwellung grösserer Kinder ("Mastitis adolescentium")]. Stern (G.), Ztschr. f. ang. Anat. [etc.] (Berl.), 1920, **6**, 367-374.

Because of the neurasthenic manifestations, it is argued that a constitutional neuropathy is a primary factor in mastitis of adolescent children. The endocrine metabolic disturbances are considered secondary to these nervous components. A few references to literature are given.—A. T. R.

Opotherapy and the MENOPAUSE (Opothérapie et ménopause). Opotherapy and minor Graves' disease (Opothérapie et petit Basdowisme). Marie (A.) & Fourcade, Bull. Soc. de thér. (Par.), 1921, 4, s. **26**, 52-56; 176-178.

Marie and Fourcade state that suppression of the monthly periods is not the only cause of such mental disorders at the menopause as obsessions, phobias, melancholia, acute hallucinations, and more or less systematized persecutional insanity which occurred at this time. They were inclined to assign the chief rôle to endocrine insufficiency, especially of the thyro-ovarian secretion. They therefore made a systematic use of opotherapy in all the mental disorders of the menopause. After a preliminary period of 10-15 days devoted to a general disintoxication, when a slight degree of hepato-renal intoxication was present, a combination of **thyroid** and **ovarian** extract was employed, supplemented by **suprarenal** extract or extract of other **endocrine organs** whenever signs were present indicating their insufficiency. The histories of eight cases are recorded, in six of which considerable improvement took place under this treatment and in two no result was obtained. Subsequently Marie and Fourcade reported 10 cases with minor signs of Graves' disease that were benefited by pluri-glandular opotherapy consisting in administration of extracts from the ovaries, **corpus luteum** and **hypophysis.**—Med. Sci., **5**, 309.

(ORGANOTHERAPY) A suggested form of treatment for mental deficiency in children. Miller (J. A.), New York M. J., 1921, 114, 231-232.

The author assumes that the rather prevalent and wide attempts to treat mental deficiency in children with glandular extracts is irrational. "We cannot stimulate a dead body or an absent one."—H. W.

(ORGANOTHERAPY) The treatment of the vomiting of pregnancy by thyro-ovarian opotherapy (Le traitement des vomissements gravidiques par l'opothérapie thyro-ovarienne). Naamé, Bull. Soc. de thér. (Par.), 1921, 4.s. **26**, 180-182.

According to Naamé, of Tunis, the vomiting of pregnancy is due to autotoxemia caused by thyro-ovarian insufficiency, and the cessation of vomiting towards the middle of pregnancy is the result of establishment of glandular equilibrium owing to hypertrophy of the **thyroid.** A rapid cessation of vomiting can be effected by thyro-ovarian opotherapy, which favors the development of this hypertrophy. The treatment consists in administration of tablets containing thyroidin 0.05 gm. and **ovarian** extract 0.10 gm., three times a day for a few days.—Med. Sci., **5**, 310.

OVARY grafting in clinical practice (Over de klinisch overplanting van ovarium weefsel). de Bruyne (F.), Vlaamsch geneesk. Tijdschr. (Gent), 1922, **3**, 37-39.

To diminish as much as possible the complaints after hysterectomy and after complete ovariectomy the author recommends the

transplantation of a piece of ovary subcutaneously. This does not give as splendid results as the transplantation in the peritoneum, but when for one reason or another the graft must be removed no laparotomy is necessary. In ±50 per cent of the cases the graft disappears; in the other cases the issue grows and forms cysts. When only **corpus luteum** is transplanted, hypertrophy is rare; transplantation of the cortex gives most cases of hypertrophy. Transplantation of corpus luteum alone very seldom has any influence on the climateric complaints; when the graft consists of the cortex only, it nearly always has a very good influence on these symptoms. Therefore it is of special importance that the graft contain a large quantity of cortex tissue.—J. K.

Transplantation of OVARY (Overientransplantation). Fleischmann (K.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 245.

A short article. The indications for operation were amenorrhea, sterility and vasomotor disturbances. The author does not state whether the operation was successful.—J. K.

The comparative value of whole OVARIAN extract, CORPUS LUTEUM extract, and ovarian residue in menstrual disorders. Hirst (J. C.), N. York M. J., 1921, **114**, 391-394.

The extract of the whole ovary is most useful in the treatment of the menopause, both natural and surgical, and the late establishment of menstruation. The best method of administration is by deep muscular or intravenous injection. Nausea is a common complaint following administration by mouth. If the extract is given by mouth the dose should be five grains three times a day midway between meals, combined with one-fortieth of a grain of strychnine sulphate. When ampoules are used the amount should be 1.0 cc. to each injection (intramuscular) daily for thirty-six doses. The series may be repeated after one or two months, if necessary. The intravenous injection is preferable at times because of the rapidity with which adequate amounts can be given and the absence of local reactions. Certain protein-sensitive individuals will show some systemic reactions, such as diffuse patches of erythemia, urticaria and occasionally headache. The indications for the use of ovarian residue are late development of puberty, infantilism, irregular menstruation at puberty, menorrhagia of puberty, obesity and amenorrhea-dystrophia adiposo-genitalis. The methods of administration of ovarian residue are the same as those for whole ovarian extract. "The results of this extract are still in the nebulous stage, as far as proof is concerned." Corpus luteum is used to control the nausea of pregnancy, habitual abortion without demonstrable cause, menopause (in which it is not as efficient as ovarian extract), scanty menses or functional amenorrhea of youth, pruritus vulvae or krau-

rosis vulvae in elderly women, and sterility. The administration of corpus luteum is the same as for the two preparations mentioned above. The nausea of pregnancy is relieved by a series of 12 intramuscular or intravenous doses in mild cases or two doses daily of 2.0 cc. amounts in severe cases. The presence of **goiter** in early pregnancy absolutely contraindicates the administration of corpus luteum extract, either intravenously or intramuscularly. ". . . Every such patient has been made worse by this treatment."

—H. W.

(OVARY) The existence of yellow atretic bodies in the interstitial gland of the rabbit (Sur l'existence de faux corps jaunes autonomes dans la glande interstitielle de la lapine). Salazar (A.), Anat. Record (Phila.), 1922, **23**, 189-193.

The author calls attention to the existence in the ovary of the rabbit (ovary of the interstitial type) of yellow atretic bodies, with autonomous evolution; these, unlike the ordinary atretic bodies, do not amalgamate in the interstitial gland, but pass through their evolution autonomously, isolated within a connective-tissue capsule. The author briefly describes their characteristics and admits the possibility of their being confused with genuine old yellow bodies, this confusion being possibly one of the causes of the contradictory opinions that have been formulated with regard to the regression of the real bodies.—Abst., Wistar Institute.

Function of the OVARY during gestation (Fonctionnement des ovaires pendant la gestation.) Vignes (H)., Progrès méd. (Par.), 1922, **37**, 49-52.

A review of the literature leads the author to the following conclusions. The ovaries increase in size during gestation, the **corpus luteum** becomes harder and larger than it is at the time of menstruation, and there are a considerable number of follicular atresias. Ovulation is usually suspended, but there are exceptions to this rule; the function of menstruation ceases during gestation. The secretion from the ovary acts upon the mucous membrane of the uterus to bring about premenstrual congestion, the condition necessary to nidation. For a certain length of time the ovary keeps the mucous membrane of the uterus in a condition which is indispensable to the development of the embryo. This sensitization of mucous membrane and this role of protection are attributed particularly to the corpus luteum. Injury to or disfunction of the ovary may cause pathological conditions in the course of gestation.—R. G. H.

(OVARY) Dysmenorrhea. Young (J. Van D.), N. York M. J., 1921, **114**, 395-397.

True dysmenorrhea may be looked upon as the result of two conditions: (1) a deficient ovarian function associated with a normal

myometrium—a condition which permits of a profuse clotted flow; (2) a degenerated uterine wall which causes a mechanical barrier to uterine circulation—a condition which produces a scanty flow and cramps. Pain in the first condition may be looked upon as the result of unhormonized blood clotting (normal menstrual blood does not clot and will prevent other blood from clotting), and in the second condition to muscular spasms. In either condition the endometrium has no part in the causation of pain; the endometrium seldom is a causative factor in dysmenorrhea. The author has devised a treatment which consists in the production of rhythmical uterine stimulation on the Bier's hyperemia principle.—H. W.

The internal secretion of the PANCREAS. Banting (F. G.) & Best (C. H.), J. Lab. & Clin. M. (St. Louis), 1922, **7**, 251-266.

The authors attempted to secure extracts of Langerhans islet tissue from the pancreas in the hope that it would give hormone effects uncomplicated by the action of enzymes. It was found that intravenous injections of extract from dog's pancreas, removed from seven to ten weeks after ligation of the ducts, invariably exercised a reducing influence upon the percentage of the **blood sugar** and the amount of sugar excreted in the urine. Rectal injections were not effective. The extent and duration of the reduction varied directly with the amount of extract injected. Pancreatic juice destroyed the active principle of the extract. That the reducing action was not a dilution phenomenon was indicated by the following facts: (1) hemoglobin estimations before and after administration of extract were identical; (2) injections of large quantities of saline solution did not effect the blood sugar; (3) similar quantities of extracts of other tissues did not cause a reduction of blood sugar. Extract made 0.1 per cent acid was effectual in lowering the blood sugar. The presence of extract enabled a diabetic animal to retain a much greater percentage of injected sugar than it otherwise would. Extract prepared in neutral saline solution and kept in cold storage retained its potency for at least seven days. Boiled extract had no effect of reduction of blood sugar.—R. G. H.

The thermostable active agent of pig's PANCREAS. Jones (W.), J. Biol. Chem. (Balt.), 1922, **50**, 322-328.

Not of endocrine interest.—F. S. H.

The internal secretion of the PANCREAS (La sécrétion interne du pancréas). Waterman (N.), Arch. néerl. de physiol., 1920, **4**, 289-346.

Alcoholic extracts of the pancreas and the change in viscosity of blood are used as a measure of the lipins. The internal secretion of the pancreas consists in the production of a complex lipoid, an

unstable lipoid-phosphatide, which dissociates and liberates free fatty acids. This lipoid influences the permeability of the cellular membranes; it regulates glycogenesis and the excretion of sugar by the kidney. The factors which influence the dissociation of this complex lipoid, and likewise the formation of intermediary compounds of carbohydrates, are heat, **adrenaline** and chloroform.—Chem. Absts. **14**, 2945.

Transplantation of PARATHYROIDS in post-operative tetany (Epithelkörperverpflanzung bei postoperativer Tetanie). Borchers (E.), München. med. Wchnschr., 1921, **68**, 1609-1612.

It is not always possible to avoid post-operative tetany because: (1) in goiter the parathyroids are often not normally situated; (2) the parathyroids mainly get their blood from the inferior thyroid artery, which must be ligated for the operation; (3) when malignant growths are present it is impossible to avoid removing the parathyroids. Often the first symptoms of tetany are observed only many weeks after the operation. Homoioplastic transplantation of parathyroid and histological examination before transplantation are necessary to make sure that the organ is a real parathyroid. Such transplantation may give splendid results though it is not always successful. The author quotes a case of a woman who was operated upon in 1882 and who died in 1919. At post-mortem examination it was found that a parathyroid that had been grafted into the liver was perfectly normal and had even become larger.
—J. K.

(PARATHYROID) An undescribed condition of infancy and its treatment. Clark (G. H.), Glasgow M. J., 1920, **94**, 193-202.

Clark, of Glasgow, describes two cases in children aged 15 months and 2½ years whose principal symptoms were idiocy, depression, fibrillary twitchings in the muscles, jerking movements in the limbs, convulsions and inability to balance. Considerable improvement took place in both cases under treatment with parathyroid gland tablets. The symptoms were very similar to those observed by Paton and Findlay after thyro-parathyroidectomy in animals, hence Clark's cases were probably examples of parathyroid tetany. —Med. Sci., **5**, 305.

(PARATHYROID) Du rôle du calcium dans la tetanie. Kummer (H.), Presse méd. (Par.), 1920, **28**, 765-766.

The cases are reported of two patients in whom the ingestion of citric acid brought on severe attacks of tetany. This effect is ascribed by the author to calcium deprivation due to the formation of calcium citrate. He believes that calcium depletion deprives the body cells of defense, leaving them more vulnerable to the toxin that brings about parathyroid tetany.—R. G. H.

The prevention and control of PARATHYROID tetany. Luckhardt (A. B.) & Rosenbloom (J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **19**, 129-130.

To test the hypothesis that parathyroid tetany is due to accumulated toxin, the authors determined the effect of copious diuresis on the process. Ringer's solution or the same without calcium was injected intravenously in amounts of 33 cc. or more per kilo. Animals were kept alive in good state of nutrition for long periods (up to 51 days). Typical tetany supervened when diuresis was discontinued and meat diet maintained. The presence of calcium in the injected fluid appears to have been of little significance.—R. G. H.

Transplantation of PARATHYROID in paralysis agitans (Behandlung des Paralysis agitans mit Epithelkörperimplantation). Sudeck, Deutsch med. Wchnschr. (Berl.), 1922, **48**, 210.

The effect of this operation is due only to suggestion.—J. K.

(PARATHYROIDS) Calcium metabolism in tetany. Underhill (F. P.), Tileston (W.) & Bogert (L. J.), J. Biol. Chem. (Balt.), 1922, **50**, xxxix.

When compared with normal individuals under the same experimental conditions a subject with tetany, presumably of gastrointestinal origin, showed a normal type of behavior to calcium intake except that there was evidence of a greater tendency to store calcium temporarily on a calcium-rich diet. On the other hand, on a calcium-poor diet this stored calcium was eliminated to a much greater extent than occurred in the normal subject. These facts may, perhaps, be interpreted to mean that the organism with tetany shows a greater need for calcium than the normal individual, but that in tentany the regulation of calcium equilibrium is in an unstable condition.—F. S. H.

Mixed tumor of the PINEAL gland (Ein Beitrag zu den Mischtumoren der Zirbeldrüse). Frank (M.), Ztschr. f. ang. Anat. [etc.], (Berl.), 1921, **8**, 65-78.

Detailed description of autopsy findings in a 20-year-old man with a large (34x24x22 mm.) mixed and partly cystic tumor of the pineal gland. Literature.—A. T. R.

Un cas de SCHLERODERMIE. Hugel, Réunion dermatologique de Strasbourg, Jan. 8, 1922; abst. Presse méd., **30**, 154.

The case was presented of a man of 45 who showed marked scleroderma of the lower limbs. The condition was ameliorated by the use of "fibrolysine" supplemented with pluriglandular organotherapy.—R. G. H.

SCHLERODERMIE et opothérapie associée. Lereboulet (P.), Bull. et mém. Soc. méd. d. hôp. de Par., 1921, 3.s., **45**, 1200-1204.

Lereboullet reports three cases showing the benefit obtained in cases of sclerodermia by the association of **thyroid, pituitary,** and **suprarenal** extracts.—Med. Sci., **5**, 310.

Antitoxic action of SECRETIN from spinach for strophanthin (Ueber die entgiftende Wirkung der Spinatsekretinlösung auf Storphantin). Miyadera (K.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 313.

When secretin, extracted from spinach as described by Bickel, was added to strophanthin the toxicity of this substance was largely decreased.—J. K.

A suggestion as to the cause of the aspermatic condition of the imperfectly descended TESTIS. Crew (F.), J. Anat. & Physiol. (London), 1922, **56**, 98-106.

The author holds that the imperfectly descended testis is aspermatic because the temperature of the abnormal position is higher than that which is normal for the scrotum. The latter is conceived to be the optimum temperature at which the final stages of spermatogenesis take place.—W. J. A.

Hypoplasia of the TESTES during the period of development (Über die hypoplasie der Hoden in der Entwicklungsperiode). Diamantopoulos (S.), Ztschr. f. ang. Anat. [etc.], (Berl.), 1921, **8**, 117-154.

Ninety-nine pairs of testes from new-born (some premature and some full term) to boys 18 years of age, were examined histologically. The normal testis at birth has wide tubules and practically no interstitial tissue. Testes with narrow tubules and interstitial tissue are considered underdeveloped. Of these 99 pairs, 60 were underdeveloped (37 very pronounced and 23 only slightly). Two of these undeveloped testes had no interstitial cells while in the rest this tissue was moderate or small in amount. No direct relationship was found between development of the tubules and amount of interstitial tissue. Puberty apparently brings many of these undeveloped testes nearly up to normal. Of the 34 cases of **status lymphaticus** and **thymolymphaticus**, 21 had underdeveloped testes and in 13 they were normal. Seven cases showed, besides abnormal sexual development and status lymphaticus, **suprarenal** hypoplasia (4 with both cortex and medulla and 3 with only cortex). There were 5 cases with hyperdevelopment of the **thyroid.** Boys with underdeveloped testicles are less resistant to infections and other disturbances, which probably explains the large number of cases of hypogenitalism in dead children. Hypoplasia of the testes

inhibits the growth of the prostate and seminal vesicles. Diseases of the mother had apparently no bad effect on the testes of the fetus. A long list of references is given.—A. T. R.

Proliferation of the interstitial cells in chorionepithelioma of the TESTIS (Über Wucherung der Leydigschen Zwischenzellen bei Chorionepitheliom des Hodens). Hedinger (E.), Ztschr, f. ang. Anat. [etc.], (Berl.), 1920, **7**, 55-59.

The case is that of a 29 year old man who died from multiple metastasis one month after the right testis had been removed because of a chorionepithelioma of the right testis. The left testis was found to be normal except for a great increase in the interstitial cells as compared with the testes of about 100 influenza cases between 25 and 35 years old, which the author used as control material. In three cases (soldiers from 25 to 35 years of age) of unilateral castration of long standing there was no such increase in the interstitial cells of the remaining testis. Attention is drawn to a similar situation in the female where chorionepithelioma of the uterus is related to proliferation of lutein cells in the ovary. No literature.—A. T. R.

(TESTES) Partial castration (Sur les conséquences de la castration partielle). Lipschütz (A.), & Ottow (B.), Compt. rend. Soc. de biol. (Par.), 1920, **83**, 1340-1341.

As a result of studies on a rabbit and three guinea-pigs the authors conclude that a small remaining fragment of a normal testis ($\pm\frac{1}{16}$ the normal weight) can furnish the organism the quantity of internal secretion necessary to the development of normal sexual characters. But a diminution of the quantity of the internal secretion during the development of the organism can result in retardation of development of the sexual characters. If only a part of the testis is left augmentation of the total weight of the rest of the testis does not take place. It is very probable that the germinative tissue in the testis is in a state of degeneration as after the ligation of the vas deferens. It is very probable that the interstitial tissue in the divided testis is increased in size. That is why the number of interstitial cells, the cells in which internal secretion is formed, is not very much decreased in partial castration.—R. G. H.

So-called mixed-tumors of the TESTICLE (Sui cosidetti "tumori-misti" del testicalo). Renato (M.), Morgani (Milano), 1921, **64**, 375-385.

Of no immediate endocrine interest.—J. K.

Transplantation of TESTICLE (Hodenüberpflanzung). Rosenthal (H.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 209.

A short article. An operation is indicated in very few instances; desire for rejuvenation is no indication. In Germany there seems to be a regular trade in testicles, some persons offering to sell one of theirs.—J. K.

The supposed relation between alkalosis and TETANY and similar conditions. Greenwald (I.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **18**, 228-234.

This is a technical discussion of literature and of personal findings. Doubt is cast upon the current hypothesis that alkalosis may form an important part in the genesis of tetany.

—R. G. H.

(THYMUS) Observations on the effect of hyperthymisation (Beobachtungen über die Folgen der Hyperthymisation). Demel (R.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1922, **34**, 437-449.

The author removed the thymus from rats of 3 weeks, 2 months and 8 months, respectively, and transplanted the organs into young rats. After the grafting marked adiposity developed and the animals were very lively and vigorous. The growth of the bones in length increased after implantation of a thymus. The thymus of animals of 3 weeks or 2 months is more active than the thymus from rats of 8 months. Even the influence of the thymus from other animals cannot be denied. The epiphyses of the bones of the rats in which the thymus is implanted is broader than in control animals. The structure of the bone becomes much more compact after implanting a thymus. The transplantation has no influence on **adrenals, gonads or hypophysis.** Administration of thymus by mouth has no influence on rats.—J. K.

Congenital bone fragility and the THYMUS. Contribution to the study of bone dystrophies in relation to the endocrine glands (Fragilità ossea congenita e timo. Contributo allo studio delle distrofie ossea in rapporte con le ghiandole endocrine). Frontali (G.), Riv. di clin. pediat. (Firenze), 1920, **18**, 257-309.

After a critical review of the literature of the subject, the author describes a case of congenital bone fragility, which has been studied in detail with all applicable modern methods. The child was observed between her first and third months of life. A first fracture was noted immediately after birth. The skull was of parchment consistency. The lower limbs were shorter than normal (18:26.5 cm.) and there were numerous callosities on all tubular bones. Blood examination showed: red corpuscles, 3,624,000; haemoglobin, 80%; white corpuscles, 7,500; lymphocytes, 63.5%; transitional forms, 3.5%; neutrophile polynuclear cells, 25%; eosinophiles, 1%; basophiles, 0.5%. Galvanic excitability of several

muscles was found diminished, with little difference between anode and cathode; sometimes the formula was inverted. Calcium retention for 3 days averaged 26%; the calcium content of the blood (weighed as CaO) was 0.2866%, both being approximately normal. Radioscopy showed bone translucency increased throughout; the delicate outline of the cortex was partially interrupted; epiphyseal lines were normal.

Death from pneumonia occurred and a necropsy was made. The thymus was reduced in volume and weight (3gm.), grey in color, and sclerotic. The total number of bone fractures was 33. In tubular bones the epiphyseal ossification zone was normal, the compact layer, completely missing. It appeared as though absorption of the embryonic fibrous bone tissue had failed to occur. There was no cortical compact layer, but a calcification of the thickened periosteum. Numerous other details as to bone are recorded. In the thymus connective tissue was considerably increased. Groups of epithelioid cells and of Hassal corpuscle were isolated by fibrillar rings. The internal structure of the lobuli showed a diminished number of epithelioid cells with poorly stained protoplasm—in short, sclerosis with lymphoid degeneration and atrophy of the epithelioid elements. The thyroid was slightly hyperplastic but otherwise normal, as were the hypophysis and adrenals. The degeneration of the thymus is considered as etiologically related with the bone dystrophy. Congenital fragility of the bones, a definite entity of prenatal origin, must be differentiated from such conditions as rickets, etc. The cases in the literature which were not complicated by rickets were characterized by severe periosteal aplasia. The case described showed a complete absence of compact cortical bone and other evidence of insufficient activity of osteoblasts. Osteoclasts were rare. Therapeutic injections of serum of children with normally functioning thymus is proposed.—Author's abst. abbreviated.

Variations in the form and position of the THYMUS (Über Variationen der Thymusform und -lage). Gruber (G. B.), Ztschr. f. ang. Anat. [etc.] (Berl.), 1920, **6**, 320-332.

Description and 13 illustrations of various types of persistent thymi found in new-born and very young children, with a discussion of their rôle as mechanical factors in so-called thymic death. It is considered possible that this might be brought about by compression of the large vessels and trachea. Further investigation is considered necessary to decide whether hyperplasia of the thymus is always the pathologic-anatomical equivalent of hyperthymization. Some references to literature are given.—A. T. R.

Lymphosarcoma of the THYMUS [Lymphosarcome du thymus (Présentation de pièces)]. Harvier (P.), Bull. et mém. Soc. méd. d. hôp. de Par., 1921, 3. s. **45**, 374-378.

Harvier reports a case of lymphosarcoma of the thymus in a woman aged 25, characterized by a syndrome indicating compression of the superior vena cava, and consisting in cyanosis of the face, edema of the front of the thorax, extraordinary development of the collateral venous circulation from the face to the pubes, as well as in a continuous cough, with attacks of suffocation and intermittent pain in the left shoulder and arm. Physical examination showed retrosternal and left subclavian dullness, left pleural effusion, no cardiac symptoms except permanent tachycardia, and no signs of bronchial compression. Death took place eight months after the first symptom, and the autopsy confirmed the diagnosis of a large tumor of a sarcomatous nature occupying the region of the thymus and involving secondarily the lungs, heart, diaphragm, liver, and kidneys.—Med. Sci., **5**, 305-306.

The influence of THYROID gland feeding upon tadpoles from which the thyroid gland and the buccal anlage of the HYPOPHYSIS have been removed. Allen (B. M.), Anat. Record (Phila.), 1922, **23**, 101-102.

Experiments were performed upon Rana sphenocephala: (1) Normal controls; (2) controls cut as for hypophysis removal; (3) thyroidless tadpoles; (4) those deprived of the buccal anlage of the hypophysis; (5) tadpoles deprived of both thyroid and buccal anlage. All were fed weighed quantities of sheep thyroid preparations. The purpose was to determine whether the influence of thyroid feeding would be the same in each case. Tadpoles in young feeding stages were employed in lots of twenty-five. It appeared that presence or absence of these glands in the tadpoles had little control upon the influence exerted by thyroid feeding upon limb development. The tail was not so quickly reduced as a result of administration of thyroid to groups 4 and 5 as in groups 1, 2 and 3. It is possible that future experiments in administering more diluted doses of thyroid preparations may prove a more delicate test. A study of the thyroid glands of controls and of tadpoles deprived of the buccal anlage of the hypophysis fails to show any modification of gland development or of colloid accumulation to result from thyroid feeding.—Author's abst.

(THYROID) The use of radiotherapy in Basedow's disease (La radiothérapie dans la maladie de Basedow). Béclère, J. méd. franç. (Par.), 1920, **9**, 302-305; Arch. d'électric. méd. (Par.), 1920, **28**, 348.

Radiotherapy is the ideal treatment for Basedow's disease and for all forms of hyperthyroidism, for, better than intervention, it destroys the secreting elements, or, at any rate, diminishes their secretory activity. When the morbid condition does not date back more than a year and the gland is soft, treatment by intensive doses

at long intervals takes only from two to three months. In chronic forms, with a hard gland to which are added hyperplastic lesions of the connective tissue, the treatment takes at least six months, and improvement remains incomplete. In simple hyperthyroidism, on the contrary, radiotherapy is always perfectly successful, but it is in serious forms with extreme wasting and intense rapidity of heart action that this method gives the best results. Irradiation should be penetrating (20 cm. equivalent spark gap, 5 mm. aluminum, 20 cm. distance from the anticathode, localizing cylinder 10 cm. in diameter), seances should be weekly, and the dose 3H. Radiotherapy should be directed towards the function and not towards the lesion, and should be guided by the disorders of circulation (frequency and inequality of the heart-beats) and avoid substituting for excess, a deficiency of the thyroid secretion.—Med. Sci., **4**, 390-391.

(THYROID) On a further series of 500 goitre operations with special reference to after-results. Berry (J.), Proc. Roy. Soc. Med. (Lond.), 1921, **14**, (Surg. Sect.) 89; Brit. J. Surg. (Bristol), 1920-1921, **8**, 413; Abst., Med. Sci. (Lond.), 1922, **5**, 324-325.

Berry devoted this paper to a careful review and analysis of his cases, including all in which he had removed any portion of the thyroid gland during the period from 1913 to 1919, inclusive. The cases were 500 in number and formed a direct continuation of a previous series. Only about 12.5 per cent of the patients were males, and the age at which the disease was most common was between 30 and 50. Five girls, however, were only 14 years old. These were all examples of parenchymatous goitres which were causing dyspnoea and failing to respond to medical treatment. Operations in children below the age of puberty were hardly ever necessary and should never be undertaken except for some specific reason. Among the male patients, 7 were over 70 years of age, and all made good recoveries. One hundred ninety-eight cases were encapsulated lesions, adenoma, or cysts, and 302 were non-encapsulated. These included 13 examples of malignant disease. Berry states that pathologically the above classification is not strictly accurate, but is convenient, clinically. He lays stress upon the inefficiency of modern classifications, but points out that the terms in use are of clinical value. The series includes only 3 cases of inflammation. There were, however, 79 operations for exophthalmic goitre, and he points out that these cases should be sharply distinguished from false exophthalmic goitres, that is, localized lesions which may give rise to tachycardia and tremor but never show any exophthalmos. Of the malignant cases some were of the papilliferous variety, one was an endothelioma, and two were sarcomata. In this group the first sign for operative interference was dyspnoea, 74 operations being undertaken for this cause. Dis-

comfort and deformity or hyperthyroidism were the next most frequent indications. He points out that dyspnoea, when long persistent, may lead to other complications, such as dilation of the heart, tachycardia, and chronic lung trouble. In no case had he to perform a tracheotomy, as he holds very strongly that the removal of the source of the pressure, namely, the goitre, is a far more satisfactory procedure. He points out, however, that after the goitre has been removed there is sometimes a danger of tracheal collapse. When the trachea is bilaterally compressed the removal of one lobe may be quite insufficient to relieve the dyspnoea or indeed may make it worse, as this may lead to kinking, which usually causes fatal suffocation. He also points out that a unilateral enlargement of the thyroid may be considered the cause of the dyspnoea, whereas the opposite lobe, which may be the real offender, may lie deep behind the sternum within the thorax. He lays stress upon the difficulties of diagnosis in doubtful malignancies and states that a positive diagnosis of malignancy is almost impossible, although there may be points which give rise to suspicion. It is important, in making a diagnosis, to determine whether the thyroid moves upon the larynx or the trachea, for in the malignant cases it is likely to be fixed. He gives a full review of the operations which have been undertaken for the different varieties of disease and also a full description of his method of removing an intrathoracic goitre. In nearly all cases drainage was employed, being omitted in only 7 of the 500 cases. There were only 2 deaths in the simple goitres, 3 in the exophthalmic goitres, and 2 in the malignant diseases. Of the 500 cases he had traced all but 14 cases. Of the total, 342 of the simple goitres, 53 of the exophthalmic goitres and 5 of the malignant cases were quite well.—R. G. H.

The fundamental classification of THYROID disease by the basal metabolic rate. Boothby (W. M.), Collected Papers Mayo Clinic (Phila.), 1921, 297-303; reprinted from J. Am. M. Ass. (Chicago), 1921, **76**, 84-86.

The measurement of the heat production in an individual under standard conditions serves to differentiate diseases into three groups: those with decreased, those with increased, and those with normal basal metabolic rates. The value, the limitations, and the essentials of technic and physiologic details are discussed.—J. F.

(THYROID) Total metabolism in exophthalmic goitre. Boothby (W. M.) & Sandiford (I.), J. Biol. Chem. (Balt.), 1922, **50**, xlvii.

The work included a quantitative study of the food intake, urinary elimination, the blood chemistry, and the respiratory metabolism in three cases of exophthalmic goitre. The total metabolism was found to be frequently in excess of 5,000 calories per day and occasionally over 6,000 calories, which is in marked contrast to the

daily food ration of 1,500 to 1,800 calories common in many countries during the war.—F. S. H.

(THYROID) Sloughing cornea in Graves' disease and in disseminated sclerosis. Buller (T. H.), Brit. J. Ophth., 1921, —, — (July).

Buller describes the case of a woman suffering from exophthalmic goitre, who had such exaggerated proptosis that the left cornea could not be covered by any effort. She rejected his advice to have the lids sutured together and a month later was seen with an infiltrated anesthetic cornea, which soon developed an ulcer and onyx. The cornea was incised and the lids sutured. In two days the sutures cut out and the eye re-opened. Cauterization failed to check the spread of ulceration and the eye was finally enucleated. The second cornea began to ulcerate, but the patient by this time was very low and soon died of heart failure.—Med. J. Australia, 1921, ii, 356.

THYROID opotherapy and tuberculosis (Opothérapie thyroidienne et tuberculose). Coulaud (E.), Ann. de méd. (Paris), 1921, **10**, 385-394.

Evidence is presented from a series of 7 cases that thyroid therapy is distinctly harmful in pulmonary tuberculosis.—F. S. H.

The reticular material as an indicator of physiologic reversal in secretory polarity in the THYROID cells of the guinea-pig. Cowdry (E.), Am. J. Anat. (Phila.), 1922, **30**, 25-37; Anat. Record (Phila.), 1922, **23**, 13.

In the thyroid glands of normal guinea-pigs, the reticular material (i. e., Golgi apparatus, canalicular apparatus, etc.) is not invariably found between the nuclei and the follicular lumen, as is generally supposed. In some cases it undergoes an active migration to the opposite pole of the cell, which, together with other evidence at hand, indicates the existence of a reversal in physiologic polarity whereby the secretion is discharged directly into the circulation, instead of being first stored within the follicles.—Author's abst.

(THYROID) Cretinism—early diagnosis. Echols (G. L.), J. M. Ass. Georgia (Atlanta), 1921, **10**, 825-826.

Echols emphasizes the desirability—and infrequency—of early diagnosis of cretinism to permit most successful treatment and forestall feeble-mindedness and insanity in later years. The symptoms regarded as most important are: (1) protrusion of tongue; (2) yellowish skin, loose and wrinkled (especially forehead); often some puffiness of the features with thickening of the eyelids, nos-

trils and lips, also of hands, feet and back of neck, due to myxoedematous swelling; (3) abdominal swelling; (4) general mental apathy and slowness of movement; (5) scantiness of hair and eyebrows; (6) snorting and snoring breathing; (7) subnormal temperature.—R. G. H.

La fonction THYROïDIENNE et la procréation. Favreau (M.), J. de méd. de Bordeaux, 1922, **3**, 87-89.

This article is a review of some of the pertinent data mostly taken from French sources. These conclusions are reached: There is often sterility in cases of confirmed exophthalmic goiter, but to a lesser degree when the syndrome is evasive. Hyperthyroidism sometimes causes gestation to be more difficult, sometimes has no effect upon it, sometimes makes it easier or, rarely, aggravates it. The course of the puerperium is always physiological. Nursing usually has a good influence on the disease. The offspring might have a **glandular syndrome, tetany** or changes in the bony structures.—R. G. H.

Relations between typhoid fever and THYROID (Ueber die Beziehungen zwischen Typhus und Schilddrüse). Fleckseder (R.), Wien. klin. Wchnschr., 1922, **35**, 34.

The author often observed that typhoid fever was much milder in patients with than without an enlarged thyroid. In Graves' disease, however, the prognosis of typhoid fever seems to be bad. A thyroiditis or strumitis after typhoid fever is not at all rare. No other infectious disease so often produces an inflammation of the thyroid. During typhoid fever the distribution of the blood in the body is abnormal, and it is well known that the thyroid is extremely sensitive to a want of oxygen. It is also generally accepted that the thyroid plays an important part in metabolism. Therefore, if the relation between typhoid infection and the thyroid is due to the defective circulation of this organ, we may also expect to find that in patients with parenchymatous goiters the metabolism is diminished instead of increased during typhoid fever. This is true; such patients lose only very little weight during typhoid. It is remarkable that the patient with goiter and typhoid fever generally shows a defective formation of agglutinins. The author has tried the effect of thyroid preparations in typhoid fever but without result.—J. K.

(THYROID) A case of Graves' disease made worse by radiation of the OVARIES (Ein Fall von Morbus Basedowi, verschlechtert durch Röntgenbestrahlung der Ovarien). Fleischner (F.), Wien. med. Wchnschr. (Wien), 1920, **70**, 2008-2010.

Fleischner, of the First Medical Clinic in Vienna, reports a case of Graves' disease in a woman aged 41, with a cutaneous edema

of the lower part of the body resembling scleroderma, in whom irradiation of the ovaries was followed by **amenorrhoea** and aggravation of the general condition. He alludes to two other cases on record in which x-ray treatment had a similar effect.—Med. Sci., **5**, 302.

(THYROID) A case of retrosternal goitre (Osservazioni sopra un caso di gozzo retrosternale). Franchini (F.), Pathologica (Genova), 1922, **14**, 121-122.

The author reports a case of retrosternal goitre pressing upon the heart and large vessels. The pulsations transmitted by the vessels as well as the x-ray picture had led to the diagnosis of aortic aneurism. The heart was pushed down into the left hypochondrium and the corresponding diaphragm was convex towards the abdomen. Other details as regards circulatory adjustments are described.—G. V.

Experiences with THYROIDECTOMY and ligation of the thyroid artery in depancreatized dogs. Friedman (G. A.) & Gottesman (J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **18**, 281-282.

Three dogs were subjected to pancreatectomy and the relation of thyroid deficiency to the resulting glycemia was studied. In the first case fractional extirpation of the pancreas resulted in marked glycosuria. After thyroid extirpation, leaving the **parathyroids** intact, the urine became sugar free and remained so until death, despite liberal mixed diet and 150 gm. glucose by stomach tube. In the second case complete pancreatectomy resulted in glycosuria and **blood sugar** of 250 mgs. Following ligation of both superior and inferior thyroid arteries, the urine became sugar free and blood sugar dropped gradually to 50 mgm. in 4 days. A third case resembled the second except that ligation of the thyroid arteries on one side only failed to reduce the sugar and that the dog died of tetany.—R. G. H.

(THYROID) Diagnosis, prognosis and treatment of Graves' disease (Diagnose, Prognose und Behandlung der Basedowschen Krankheit). Holmgren (J.), Wien. klin. Wchnschr., 1922, **35**, 47.

For the diagnosis of Graves' disease palpation of the thyroid is highly important (whether Graves' disease exists without goiter is unknown; if so, it is extremely rare). A technic for the palpation of the thyroid is given. The second symptom is tachycardia, which is not influenced by drugs. Exophthalmos is not always present in mild cases. A specific action of antithyroidin has never been observed by the author. Sodium phosphate as recommended by Kocher and the injection of sodium nucleinate often give good results.—J. K.

Hen feathering induced in male fowls by feeding THYROID. Horning (B.) & Torrey (H.), Anat. Record (Phila.), 1922, **23**, 132.

When fed thyroid daily, in doses increasing with their weight, from the age of three weeks, male Rhode Island Red chicks developed plumage of the female type, although males of this breed do not ordinarily pass through a juvenile stage characterized by plumage of the female type. The plumage of capons, usually ultramale, is not affected by thyroid feeding. Castrated females which typically develop male plumage are similarly unaffected. The primary effect of the thyroid feeding seems to be to increase the activity of the "lutear" interstitial tissue of the testis. The end result is a hen feathered male resembling in all essential characteristics of plumage the hen feathered males of the Seabright and Campine breeds.—Author's abst.

The relation of the THYROID to certain stages of metamorphosis in frog larvae. Hoskins (Margaret M.), Anat. Record (Phila.), 1922, **23**, 21.

The thyroid anlage was taken from its normal position and grafted into the tails of the larvae. When the animals had reached their maximum size and had well developed legs, the tails containing the thyroid grafts were cut off. With few exceptions these thyroidless animals completed metamorphosis. Examination of sections has been made to eliminate all cases in which thyroids regenerated in the normal position, and it was found that although a large percentage of regeneration was present, a number of the frogs were actually thyroidless. It is therefore evident that the thyroid is not directly necessary for the later stages of metamorphosis.—Author's abst.

Formation of anti-bodies in THYROIDECTOMIZED animals (Formation d'anticorps chez les animaux éthyroïdes). Houssay (B. A.) & Sordelli (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1220.

The omission of some lines in their note of July 21, 1921 (See Endocrin., 1922, **6**, 353, has obscured the sense. The anti-sheep serum furnished by thyroidectomized rabbits has a titer for hemolysins higher than the controls. The titer for agglutinins is also higher in the thyroidectomized rabbit and horse, than in the controls. The statement as to antitoxins remains the same.—T. C. B.

Some observations on goiter based on a routine study of 800 consecutive THYROID patients. Jones (E. G.), J. M. Ass. Georgia (Atlanta), 1921, **10**, 821-824.

Four per cent of the subjects were negroes, the rest white. Only 8 per cent were males, but the percentage of the toxic type was greater among men, owing to the high incidence of non-toxic

goitres in girls. Twenty-five per cent had one or more relatives with history of goitre. About half had goitre in the immediate family. No relation between water supply and goitre could be recognized. No significant correlation between pelvic disorders and goitre could be found. In the exophthalmic group the goitre was first noticed at an average age of 27.8 years. More than 50 per cent occurred before 25. Twenty per cent occurred before 18; and an additional 7 per cent are thought to have appeared at puberty, disappeared, and reappeared at ages ranging from 26 to 49. Thirteen per cent of this class thought the symptoms antedated the enlarged thyroid, while 35 per cent thought the goiter and symptoms appeared simultaneously; so that only about 50 per cent noticed the goitre before the symptoms. In the class of patients with toxic symptoms without exophthalmos the interval between the appearance of the goitre and the appearance of the symptoms is considerably longer than is the same interval in exophthalmic patients. Three cases of carcinoma were included in the series. Temporary post-operative disturbance of the voice was not infrequently seen, and a few cases of aphonia persisted from 4 to 12 weeks. A maximum amount of thyroid tissue was commonly removed at one or more operations. Recurrences have not been a significant feature. Blood pressure ranged from 90 to 240 mm. Hg. in various cases. Jones believes that hypertension is merely incidental, not symptomatic of the disease. The mortality in toxic goitre was less than 1 per cent. In the whole operative series it was 1.4 per cent. The best record was 155 operations between deaths. The mortality during the last year was 0.8 per cent.

—R. G. H.

The influence of THYROID preparations on the blood picture and especially on eosinophilic cells. Kamikozawa (Y.), Cent. J. of Med. (Japanese), No. 349; Jap. Med. World, 1921, **1**, 18-19.

The administration of thyroid preparations in 6 cases of bronchial asthma caused a decrease in eosinophils in 7-10 days. In some cases there was an initial rise. The decrease lasted very long in some cases, while in others it stopped very soon. The asthmatic and pulmonary symptoms improve with a decrease in the eosinophils. The improvement may not be radical. The results of the action of **adrenaline**, pilocarpine, atropine, etc., on the eosinophilic cell count agree with those of Bertelli, Falta and Schweeger that the drugs that increased the tension of the sympathetic nerves caused an increase of polynuclear cells and a decrease of eosinophils, while those that increase the tension of the vagal nerves produced an increase of mononuclear and eosinophilic cells.—Chem. Abst., **16**, 286.

Secretory phenomena in pathological human THYROIDS. Key (J. A.), Anat. Record (Phila.), 1922, **23**, 23.

In hyperactive thyroids the mitochondria and secretion antecedents are increased and can be studied. In a series of 50 pathological thyroids a study has been made of the mitochondria and secretion granules and vacuoles.—W. J. A.

(THYROID) Prophylaxis of endemic goiter (Prophylaxe des endemischen Kropfes). Klinger (R.), Wien. klin. Wchnschr., 1922, **35**, 35-37.

In regions where goiter is endemic it ought to be the duty of the government to give to the children in schools tablets of an iodine compound. These tablets ought also to be given as much as possible to the adults and event to patients for years after strumectomy to prevent recurrence.—J. K.

(THYROID) Struma maligna. König, München. med. Wchnschr., 1921, **68**, 1669.

The author describes an operation during which the tumor, the trachea, the jugular vein and the lymph glands had to be removed.—J. K.

(THYROID) Myxedema with pituitary enlargement (Myxèdeme moyen et réaction hypophysaire). Mauriquand (M.) & Barre, Presse méd. (Par.), 1922, **30**, 86.

Report a child 22 months old, presenting features of typical myxedema and hydrocephalus. The tongue is hypertrophic and interferes with deglutition; the thymus is normal, the testicles are somewhat large. Urinalysis gave negative findings. The x-ray reveals an enlarged sella with effaced clinoid processes, denoting an indubitable hypertrophy of the hypophysis. Family and personal history were negative. Attention is called to the fact that an increasing number of this type of cases is being reported and to the diagnostic value of enlargement or deformity of the sella.—G. L.

(THYROID) Foreign cells in human goiters (Ueber Körperfremde Zellgebilde im menschlichen Kropf). Merk (L.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1922, **34**, 554-566.

The author sometimes found remarkable cells in goiters. Sometimes he found a large number of spores. They can be found by making a very small hole in a follicle and sucking out some liquid with a capillary pipet. If this liquid has a tobacco-like color it contains spores. Often the wall of a follicle contains brown or yellow grains in which there are enormous quantities of spores. Another cell, that is not so rare in goiters, is called by the author "rust-cell" because of its color. Cells of this sort are frequently

found in conglomerates which may be seen with the naked eye. The cells have a round or egg-shaped form and they contain a large granular nucleus. They stain with iodine or Sudan III. The protoplasm generally contains rust-colored granules. A third type, that is, however, very rarely found in goiters, is the "egg-like" cell. Cells of this sort look somewhat like eggs of helminths or cysts of protozoa. Merk has seen them only three times. Though the author is not sure, he believes that the three cells are stages in the development of a protozoon.—J. K.

(THYROID) Exophthalmos and limitation of the eye-movements of Graves's disease. Moore (R. F.), Lancet (Lond.), 1920, **ii**, 701.

There has always been doubt as to the cause of exophthalmos in Graves' disease. Moore describes the three common theories: (1) That it is due to irritation of the sympathetic nerve; (2) to engorgement of the orbit with blood; (3) to an increase of the orbital fat. He says it is still stated that the exophthalmos disappears after death, which would support the first two theories. In a case which he saw after death the exophthalmos was still present. He reports a case in which the exophthalmos was so marked that it was necessary to undertake some procedure to save the eyes. The lids of the right eye could not be sutured. He therefore made an incision through the inferior conjunctival fornix and was able to remove a large quantity of fat, after which the lids were easily approximated. He noticed that, in addition to the excess of fat, the fat itself was very edematous, as were also the inferior, internal, and external recti muscles. He deduces from this that the usual cause of the exophthalmos is an increase of fat and the limitation of movement is due partly to the pushing forward of the eye and partly to the edema of the muscles.—Med. Sci., **5**, 326.

Anti-THYROID serum. Nagaoke (H.), J. Japan Microbiol. Soc., **15**, No. 5; Jap. Med. World, 1921, **1**, 20.

Goat immune serum prepared by repeated injection of the antigen of dog thyroid precipitated the emulsion of dog thyroid. This immune serum lowered the blood pressure of the rabbit. Intravenous injection in a puppy caused dyspnea, increased heart rate and spasm of the limbs. At autopsy the thyroid, liver, kidneys and spleen were found to be hyperemic. There was dilation of the blood vessels of the thyroid and an increase of the colloidal substance in the vascular net-work, also slight degeneration in the liver and kidneys.—Chem. Abst., **16**, 287.

(THYROID) Patients treated with radium (Inferme trattati col radium). Pascale (G.), Gazz. d. osp. (Milano), 1921, **42**, 1096.

This article describes a patient with an enormous goiter, with tachycardia and exophthalmos cured by the application of radium. —J. K.

THYROID and Graves' disease (Schilddrüse und Basedowsche Krankheit). Rautmann (H.), Med. Klin. (Berl. & Wien), 1921, **17**, 645-649, 688-690.

Rautmann, of the Freiburg University Medical Clinic, regards the tachycardia, exophthalmos, and morbid excitability of the whole nervous system, and increase of metabolism, as due to over-activity of the thyroid. Although he is convinced that the thyroid plays a leading part in the pathogenesis, he admits that Graves' disease may sometimes be caused by an abnormal stimulation of the nervous system, the over-action of the thyroid being secondary. Moreover, owing to the intimate relationship of the ductless glands with one another, he thinks it possible that involvement of another endocrine organ such as the **thymus** may be the primary cause of the development of Graves' disease.—Med. Sci., **5**, 301.

(THYROID) Graves' disease and the war; a critical review of the emotional origin of the exophthalmic goitre (La maladies de Basedow et la guerre: critique de l'origine émotive du goitre exophtalmique). Roussy (G.) & Cornil (L.), Presse méd. (Par.), 1920, **28**, 753-756.

In a critical review of the emotional origin of Graves' disease, Roussy and Cornil state that only seven or eight cases which have been published in France, and a few in other countries, can be regarded as supporting this theory. In none of the cases could they find that a sudden emotion had given rise to the disease. Several other neurologists, such as Barré, Crouzon, Lépine, and Lhermitte, who had been in charge of special centres during the war, had also declared that they had never seen a typical case of exophthalmic goitre following a war condition. Roussy and Cornil therefore regard it as a mistake to insist on making emotion responsible for a syndrome in which the emotional state represents the effect rather than the cause.—Med. Sci., **5**, 301.

(THYROID) The occurrence of retrobulbar neuritis in Graves' disease (Über einen Fall von Neuritis nervi optici retrobulbaris als Frühsymptom der Basedowschen Krankheit). Sattler (H.), Wien. med. Wchnschr. (Wien), 1921, **71**, 1084-1088.

According to Sattler, of Leipzig, the occurrence of retrobulbar neuritis in Graves' disease is very rare, and has not hitherto been described as an initial symptom. He records a case of Graves' disease in which a diminution of visual acuity was the first thing that induced the patient to seek medical advice. All other possible causes of the neuritis could be excluded, and resection of the thy-

roid simultaneously benefited the retrobulbar neuritis, exophthalmos, and other symptoms of Graves' disease. A few other cases have been reported in which on improvement of Graves' disease the optic neuritis subsided. There are also cases on record of misuse of thyroid tablets being followed by retrobulbar neuritis, and finally Sattler found that experimental administration of thyroid tablets to animals produced a disease of the optic nerve resembling toxic amblyopia.—Med. Sci., **5**, 302.

(THYROID) Struma maligna. Schaedel, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 209-210.

Reported elsewhere.—J. K.

(THYROID) Graves' disease (La critica clinica del Basedow). Schiassi (B.), Policlin. (Roma), 1920, **27** (Sez. chir.), 126-145; Abst. Med. Sc., **4**, 341-342.

It is estimated that the medical treatment of exophthalmic goitre results in cure in 60 per cent of the cases. Resort to operative measures, when this treatment fails, is contemplated with some reserve in view of the possible occurrence of such accidents as tetany, hemorrhage, and collapse, which are liable to follow the operation. From a study of his own cases Schiassi considers that these accidents may be avoided if suitable precautions are taken and he recommends that whenever a fair trial of medical treatment is not followed by decided improvement, operation should be considered. The only operation that he regards as satisfactory is partial excision of the gland. He has used the methods of bilateral excision of the cervical sympathetic and ligature of the thyroid artery in several cases, but has found that in nearly half recurrence happened. On the other hand, in 37 cases of partial excision immediate cure resulted, and in 28 of these the operation has been performed sufficiently long to justify the inference of a permanent cure. He attributes these good results partly to a careful technique, but attaches particular importance to the choice of suitable cases and the proper preparation and after-treatment of the patients. In selecting cases for operation it is indispensable to ascertain the condition of the myocardium by repeated examination. The degree of regularity in the cardiac rhythm and in the tension of the pulse, and the amount of dilation both of auricles and ventricles are the points to which attention should be chiefly directed; fluoroscopy is valuable. In Graves' disease the circulatory symptoms are often transitory; when permanent, myocarditis is suggested, hence operation should not be undertaken. Other contra-indications are serious gastric crises, profuse and protracted diarrhoea, and chronic diffuse edema. The author also attaches much importance to signs of any considerable degree of paresis of the parasympathetic system, persistent paresis of the ocular

muscles (ptosis, strabismus), marked tachycardia persisting during sleep, and general asthenia, uninfluenced by medical treatment. In presence of these symptoms death during or after the operation would be a likely event. Schiassi considers that rest in bed for eight or ten weeks preceding operation is indispensable, and isolation desirable, to insure perfect physical and mental tranquillity. Small doses of morphia and veronal should be given every evening, and during the day time canabis indica, belladonna, and valerian have been found useful. As the time for operation approaches it is desirable to retain an abundance of liquid in the body, and hence the usual pre-operative purgative is omitted, water is given freely by mouth, and during the last two days, also, Locke's solution per rectum. Local anesthesia should be avoided, since it does not preclude the possibility of some mental excitement on the part of the patient. Skillful ether anesthesia is advantageous and morphia is a useful adjuvant. The post-operative treatment is analogous to the pre-operative, and should provide complete and prolonged isolation and avoidance of emotional disturbance. The action of the heart is usually upset for the first few days and morphia may be given with considerable freedom. Repeated enemas of potassium bromide and of Locke's solution are also of value. Finally, the circumstances which were the determining causes of the disease should be eliminated.—R. G. H.

(THYROID) Treatment of Graves' disease (Zur Behandlung der Basedowschen Krankheit). Schloeszmann, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 244.

Only the disease with exophthalmos, tachycardia and goiter should be called Graves' disease. Treatment may be by internal or by surgical methods. In either case, perfect rest is very necessary. Antithyroidin may give temporary improvement only. X-ray treatment sometimes improves, sometimes aggravates the condition. Internal treatment is used in the "formes frustes" only, and in patients in whom the disease is so serious and acute that operation is impossible. In all other cases, the author recommends operation in the first six months of the disease. Removal of the thymus is not recommended.—J. K.

Embryology of the derivatives of the pharyngeal pouches and the THYROID gland in the lapwing [Die Entwicklungsgeschichte der Schlundtaschenderivate und der Thyreoidea beim Kiebitz (Vanellus cristatus Meyer)]. Sicher (Lydia), Ztschr. f. Anat. u. Entwicklngsgesch. (Berlin), 1921, **62**, 233-270.

Of morphological interest only.—A. T. R.

(THYROID) Myoclonus and Graves' disease (Myoklonie und Glandula thyroidea). Simmonds (O.), Med Klin. (Berl. & Wien), 1920, **16**, 1113-1114.

Simmonds, of Frankfort, records two cases of myoclonus in women aged 22 and 28, in whom the condition was cured by thyroid gland tablets, which were given because, in addition to the myoclonus, symptoms were present in both cases that indicated thyroid insufficiency. The theory that myoclonus is due to auto-intoxication especially affecting the thyroid is thus confirmed by these two cases.—Med. Sci., **5**, 304-305.

(THYROID) Syphilis as a cause of goiter (Syphilis van de schildklier). Smit (J. H. R.), Nederl. Tijdschr. v. Geneesk. (Amst.), 1921, **i**, 156-159.

Smit records two cases of toxic thyroiditis due to syphilis with all the symptoms of Graves' disease in women aged 34 and 52, respectively, who were both completely cured by a course of anti-syphilitic treatment.—Med. Sci., **5**, 302.

(THYROID) Statistical study of simple and toxic goiter at Jefferson Barracks, Mo. Smith (F. M.), J. Am. M. Ass. (Chicago), 1919, **72**, 471-472.

Being itself a summary, the article is not amenable to abstracting. It should be read in the original by those interested in the statistics of goiter. The study is based upon examination of 65,507 men from 15 states.—R. G. H.

(THYROID) A study of the correlation of the basal metabolism and pulse-rate in patients with hyperthyroidism. Sturgis (C. C.) & Tompkins (Edna H.), Arch. Int. Med. (Chicago), 1920, **26**, 467-476.

In a study of 496 basal metabolism determinations on 154 patients with hyperthyroidism, Sturgis and Tompkins found tachycardia of 90 or more to the minute associated with a basal metabolism of +15 per cent or more in all but 16 per cent. In 70 instances where the metabolism fell to normal there was a simultaneous fall in pulse-rate in 78 per cent to below 90. In 52 patients in whom a number of metabolism determinations were made the pulse-rate gave an accurate idea of the course of the disease as compared to the basal metabolism in 85 per cent. In a series of 107 hospital patients with various diagnoses and normal basal metabolism only 5 had a heart-rate of 90 or more to the minute. There was in general an interrelationship between the pulse-rate and metabolism when a group of individuals was considered; in other words, an extreme degree of tachycardia suggested a greatly increased metabolism, while a slight tachycardia usually indicated a slight or moderate increase. The fact that a pulse-rate below 90 per minute is seldom and below 80 per minute is rarely associated with an increase in metabolism is regarded by Sturgis and

Tompkins as of great practical importance in the recognition of a large group of nervous patients who have symptoms similar to those occurring in hyperthyroidism.—Med. Sci., **5**, 303.

Interrelation of THYROID and PITUITARY in producing metamorphosis. Swingle (W. W.), Anat. Record (Phila.), 1922, **23**, 41.

Data given elsewhere.

Experiments with necturus and axolotl THYROIDS. Swingle (W. W.), Anat. Record (Phila.), 1922, **23**, 100.

Data elsewhere.

The THYROID glands of perennibranchiate amphibians. Swingle (W. W.), Anat. Record (Phila), 1922, **23**, 106.

No thyroids could be found in Typhlomolge. The thyroid glands of tadpoles with prolonged larval lives have a meager blood supply compared with adult urodeles.—W. J. A.

(THYROID) Incomplete Graves' disease with small tumor and metastases in the bones (Syndrome de Basedow incomplet chez une malade ayant une petite tumeur thyroïdienne avec métastases osseuses). Tixier (L.) & Duval (H), Bull. et mém. Soc. méd. d. hôp. de Par., 1921, 3.s, **45**, 874-876.

A case of malignant tumor of the thyroid with metastases in the bones is reported by Tixier and Duval. As is the rule in such cases, as shown by Lenormant, the picture of Graves' disease was incomplete, tachycardia and tremor being present and exophthalmos absent.—Med. Sci., **5**, 302.

The influence of THYROID and of temperature on metamorphosis of tadpoles (L'azione della nutrizione tiròidea sullo sviluppo delle larve di anfibî, sotto l'influenza di temperature varie). Terini (T.), Monitore zool. ital. (Firenze), 1919, **30**, —, —; Abst., Schweiz. med. Wchnschr. (Basel), 1920, **50**, 1102.

Terini fed larvae of Bufo vulgaris with thyroid substance. Some experiments were carried out in an incubator at 28° C. and others at room temperature from 9-15° C. The heat increased the reaction to thyroid feeding very noticeably, irrespective of the stage of development at which it was begun. The influence of the two factors is on the whole similar. Both hasten differentiation, without influencing growth. The metamorphosis proceeds rapidly. The larvae, however, remain small as compared with those developing under normal conditions. Although the increased temperature and the thyroid feeding mutually reinforce each other the high temperature alone does not produce precipitate and unharmonious development as does thyroid feeding.—R. G. H.

The function of THYROID gland with special reference to the effect of variations of diet upon it. Tsuji (K.), Acta scholae med. univ. imp. (Kioto), 1920, **3**, 713-728.

Twenty-two young rats were fed on a diet of casein 22 per cent, starch 42 per cent, cane sugar 21 per cent, lard, 12.4 per cent, salts—from incinerated rice—2.6 per cent. The materials were carefully purified. Seven rats received 2-3 cc. of milk in addition. Six young rats and six adults were also fed on unpolished rice and as much minced thyroid as they would eat. It was found that rats fed on the artificial diet alone showed arrest of growth, thus confirming results of previous authors. The thyroid glands of all these animals showed some typical histological changes, chiefly atrophy, with considerable decrease in weight. The changes of the thyroids were connected with the diminished function of the glands (hypothyroidism), which, according to the author, induced a profound change in many of other organs (**testes, ovaries,** submaxillary gland, parotid gland, **pancreas, liver** and **suprarenals**). The changes of these organs stood in contrast to those produced by thyroid feeding (hyperthyroidism). The testes of artificial diet-fed rats showed decrease in weight and diminished spermatogenesis or degeneration of the cells contained in the seminiferous tubules. The ovaries of artificial diet-fed rats were also decreased in weight and showed the degeneration of the ova and the follicular epithelia with premature ovulation. The mucous part of submaxillary gland was affected neither by artificial diet feeding nor by thyroid feeding. The typical changes were produced first in the tubuli and next in the other alveoli of the serous part both by artificial diet feeding and by thyroid feeding; while the former caused a resting state and degenerative atrophy of the glands, the latter induced activity and hyperplasia (mitoses of cells) of the glands. It is noteworthy that similar changes were produced in the parotid gland and the pancreas both by artificial diet feeding and by thyroid feeding, indicating that these two are analogous. The parotid and the pancreas of artificial diet-fed animals presented an appearance of a resting state in light cases and atrophic changes of the alveolar cells in severe cases. Thyroid feeding caused continuous activity, hyperplasia, or hypertrophy (shown by the mitoses of cells or the increase in the weight of organ), of both glands and the appearance of vacuolation in the alveolar cells. While the hepatic cells of artificial diet-fed animals were smaller and showed an increase in the amount of granules, the thyroid feeding produced a decrease of granules with the disappearance of glycogen and the appearance of mitoses. The suprarenals of artificial diet-fed animals were decreased in weight.—R. G. H.

(THYROID) The effect of iodin and iodothyrin on the larvae of salamanders. IV. The role of iodine in the inhibition of THY-

MUS-FED salamander. Uhlenhuth (E.), J. Gen. Physiol. (Balt.), 1922, **4**, 319-320.

Larvae of Amblystoma maculatum cease growing at 26 days and die at about 82 days if fed on thymus in iodine-free water. The addition of one drop of M/20 inorganic iodine to the water has no effect. Growth is resumed, however, even at 80 days, if the animals are placed upon a diet of earth worms.—M. E. C.

Simple and relatively safe THYROIDECTOMY. Van Hook (W.), Med. Rec. (N. Y.), 1921, **100**, 1072.

The writer recommends thyroidectomy with preservation of small masses of the gland at the four cornua and a thin layer of parenchyma upon the undisturbed posterior layer of the capsule. Kocher's collar incision is employed. The distinctive features of his operation are as follows: (1) The preliminary, partial hemostasis which is quite simply provided by applying light artery forceps across the whole of each of the upper cornua and across the anterior portions only of the inferior cornua. If desired, suture-ligatures may replace the forceps after pressure has been maintained for a moment. With many small artery forceps at hand, the gland-tissue is then shaved off the posterior capsule from one side of the thyroid to the other, small bleeding vessels being caught by forceps. (2) Sutures are used to close the capsule remnants by partial infolding in such a manner that only a minimum of vessels need be especially ligated. But all vessels, including the superficial veins, must be definitely closed either by this suture pressure about the capsule or by direct ligature. The method is rapid, orderly and safe.—Author's abst.

Recent researches on the THYROID (Quelques données récentes sur le corps thyroïde). Vignes (H.) & Cornil (L.), Prog. méd. (Par.), 1922, **37**, 113-116.

The article is a summary of some of the more recent evidence. It does not lend itself to abstracting.—R. G. H.